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May 16, 1947

Science

THE SCIENTISTS NEWSWEEKLY

News and Notes

Technical Papers

In the Laboratory

Stephen P. Timoshenko, professor emeritus of theoretical and applied mechanics at Stanford University, who was awarded the James Watt International Medal by the Council of the Institution of Mechanical Engineers of Great Britain on April 26. As a feature of the award ceremonies, Dr. Timoshenko delivered a series of lectures to the Institution on "Stress Concentration and Fatigue Failures." Dr. Timoshenko and the late Henry Ford are the only American recipients of the medal.

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Science and Statecraft

Marshall H. Stone

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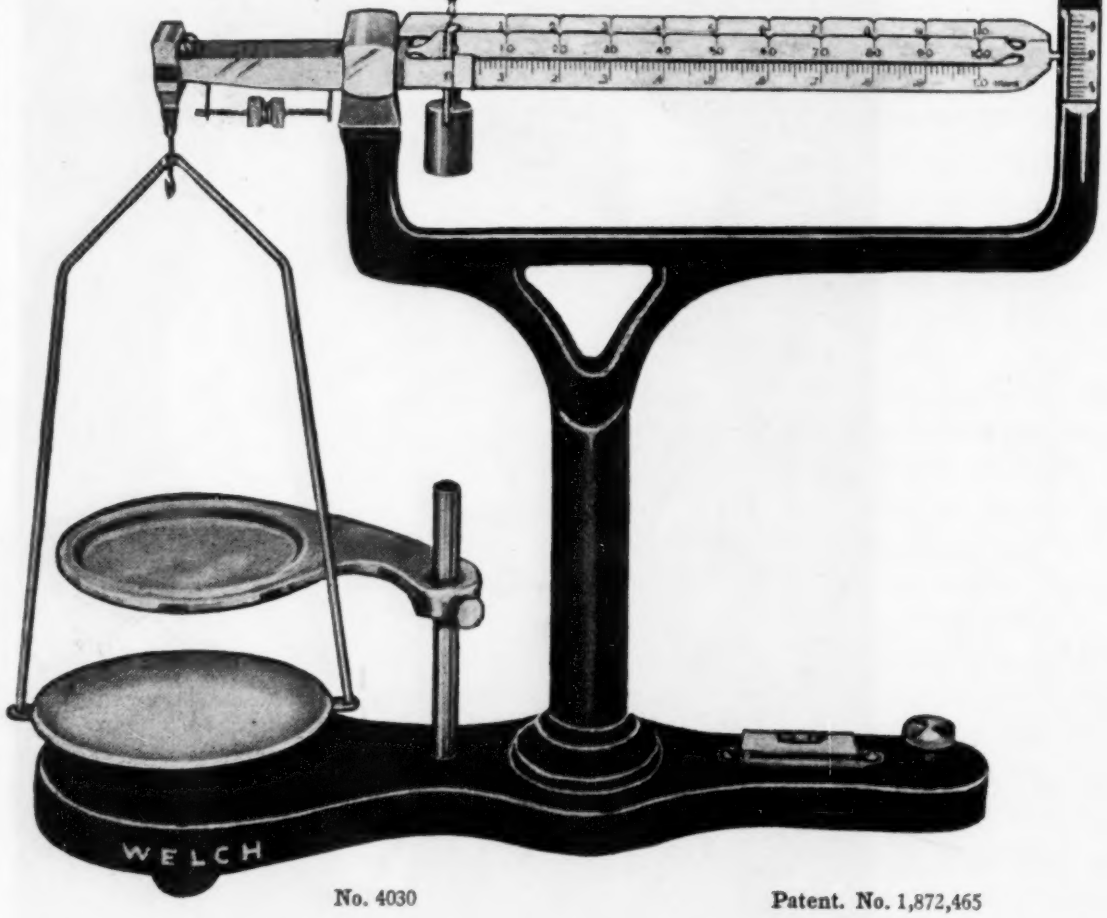

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Science and Statecraft

Marshall H. Stone

Department of Mathematics, The University of Chicago

THE EVENTS OF THE PAST FIVE YEARS have touched the lives of us all in ways both unforeseen and strange. With few exceptions we have been drawn aside from our chosen paths into activities different in kind and purpose from those naturally congenial to us. Now, as we turn our steps once more in directions fixed upon the goals we have had to abandon for a time, each of us must look upon his experiences during the war years with a still unsatisfied desire to appraise accurately their deeper significance, in both a personal and a general sense. There are few, I dare say, who do not know of lessons which could and should be drawn from their own experiences.

There must be many who share my impression that the formation of new and intricate bonds between science and statecraft is a feature of recent history which merits particularly careful analysis. The significance of developments along these lines for the scientist and the statesman, as well as for the future of mankind, needs to be comprehended, I believe, with a thoroughness which can be achieved only through the summation of limited and imperfect contributions like the one I am about to offer.

Let me begin by emphasizing the broad use I intend to make of the term "statecraft." The word "politics" in its antique acceptation would serve as well, were it not that its current meaning would introduce a certain confusion by too insistently directing attention to the minor and often ignoble tactical devices of politicians. What I wish to discuss is, rather, the high art of guiding human affairs at the level of complexity represented by the elaborately organized modern state; and I believe that in applying the term "statecraft" to this art I can suggest both its practical nature and its high place on the scale of human activity. Statecraft, thus broadly conceived, includes the handling of both domestic and foreign affairs and, by implication, also embraces the military art. It is necessary, I fear, to dwell a little upon the latter point, since it is an American habit of mind to draw a sharp distinction, practical as well as moral, between the statesman's part and that of the soldier. We are extremely reluctant to admit the lesson of history that tensions and conflicts are the rule in international affairs as in the other affairs of men; and we are even more reluctant to accept the implications of this lesson for the statesman's role in war and peace. The Teutonic directness of Clausewitz' doctrine, asserting that war is the continuation of national policy by other means, we find repellent. As for the inverted form of this doctrine, which might be phrased to assert that "peace is the opportunity for aggression by other means," even direct observation of its practical application in our times appears to fall short of carrying conviction to the American mind. Yet any objective consideration of the nature of statecraft, whether couched in universal or in national terms, must lead to the conclusion that under the circumstances of our epoch the statesman must understand both phenomenologically and theoretically the application of military force in relation to international conflicts. It is, indeed, no accident that history often reveals the great statesman and the great general combined in a single person, since the understanding of the behavior of complex societies probably meets its most direct, if not its most fundamental, challenge under the conditions of a bitterly contested war. In any event, there can be no question that the waging of a great war brings a wide range of social phenomena under a detailed scrutiny such as would normally be foregone in times of peace and which, nevertheless, provides insights of the utmost potential value for the guidance of men's peaceful affairs. It is this connection between statecraft and the military art which has particular significance in the present context, quite apart from the more basic connections mentioned above.

At no time in history, I venture to say, has our organized knowledge been brought so fully to bear upon a single, immense human undertaking as it was during the prosecution of World War II. It is hardly necessary to review the contributions made by scientists in the various warring nations to the development of military material of extraordinary variety and effectiveness, or to repeat that the fantastic achievements of science in the fields of radar, long-range missiles, and atomic explosives spell out a profound alteration of our military capabilities. To do so would, indeed, draw attention away from other aspects of the relation between science and the military art which, to my mind, have at least equal importance and which for various reasons, good or bad, still remain in relative obscurity. While it is generally recognized that a vast effort of an intellectual order was exerted in the provision of physical means for waging war, there is as yet no adequate public realization or appreciation of the comparable effort devoted throughout

Address of the retiring vice-president, Section A, AAAS, 1942, delivered at Boston, December 27, 1946.

the war to the planning and execution of military operations of every kind. Whatever appeared to be of relevance in earth science, psychology, economics, or any other branch of organized knowledge was applied for military purposes with refinements of calculation which no doubt mark a significant transformation in the military art itself. Selection and training of personnel for specialized tasks, choice and adaptation of the means to be employed under the most varied circumstances, development of tactics appropriate to the shifting realities of combat, designation of objectives at both tactical and strategic levels, analysis of the actual performance of men and of material under field conditions, and evaluation of the results achieved in specific operations were all undertaken to a surprising extent in the scientific spirit and with an extremely intelligent use of the resources of organized knowledge. In the domain of grand strategy the nature of total war manifested itself in the urgent need at all times for accurate current estimates of the total state—economic, political, psychological, and military—of each hostile power, and in the equal need for continually revised calculations of the optimum application of forces designed to encompass its eventual surrender. It is probable that no more serious or intensive attempt to arrive at a total evaluation of the dynamic state of a complex social organism has ever been made than was done under the compulsion of military necessity. It would be too much to claim that the applications made of organized knowledge were perfectly adequate to all the demands made upon it for military purposes. On the contrary, anyone familiar with one segment or another of the facts could cite many instances where relevant knowledge was overlooked, inefficiently applied, or deliberately ignored, and equally many where the imperfect state of our knowledge was clearly revealed in the light of specific military requirements.

To dwell upon such imperfections here would be both unnecessary and somewhat misleading. It is far more important to emphasize an extremely significant aspect of the rational approach to military problems which I have attempted to describe in the preceding remarks. I refer to the fact that by its very essence military planning constantly involves predictions which are subject to the immediate test of the battlefield. The ultimate penalty for error is disaster and defeat. In consequence, accuracy of observation, closeness of reasoning, and care in execution stand at a high premium in the military sphere. For all those branches of knowledge which have become allied to the military art during the recent war, this has profound implications.

It has often been observed that war accelerates and intensifies the development of new devices and new methods to an extent difficult to attain under the conditions of peace. I believe that something of the sort has occurred during the recent war with regard to the applications of science and scientific method to the problems of statecraft. In so far as those problems are of a military nature, there can be no question that the war did open up new possibilities and did afford us valuable experience in exploiting them. I have little doubt that the lessons of that experience have, at least potentially, direct significance for some of the problems of peace.

For example, the development of territories still in a wild or partly wild state, like Alaska, the Amazon Basin, or portions of Siberia, is the proper concern of statesmen and under modern conditions must apparently be contemplated in a spirit somewhat different from that which animated the explorers and pioneers of earlier generations. It seems to me reasonably clear that successful colonizing operations require organization and preparation along lines not too different from those followed by our armies in order to establish themselves in the wilderness of New Guinea. Colonization resembles a military venture even with respect to the swiftness of the retribution which may overtake erroneous appraisals of the obstacles to be mastered, as history clearly shows. A second illustration of an entirely different kind is to be found on the border line between economics and engineering, where it is becoming evident that we need a considerably improved understanding, at a strictly technical level, of the whole process of production in an industrialized society. The war confronted us with at least two major problems which made extremely heavy demands upon our knowledge in this domain: that of managing our own productive processes with maximal efficiency in relation to our total wartime requirements, and that of throttling those of our enemies in the most effective possible way with the means at our disposal, especially by strategic bombing and by submarine warfare. I believe that the experience gained in working with these wartime problems, with their definitely military character, can be used to guide our study of production under peacetime conditions for peacetime needs. If the time should ever come when it will be possible to predict with accuracy the effect upon production of variations imposed at specified points of the productive network, some of the most serious uncertainties which now confront the statesman would be removed. Some new steps in this direction can reasonably be expected in the years to come.

Leaving aside any impetus originating in the experiences of the war, I should like to suggest that there are inherent reasons why modern statecraft must move in the direction of a more scientific technique. As the integration of our great industrial societies becomes progressively tighter and their productive potentials ever greater, the acts of the statesman tend to have ever wider, deeper, and more decisive influences upon the course of events. The effects of such acts are propagated more rapidly to all parts of the social structure and are likely to be felt by the individual member of society as something of greater and more direct personal importance

than was the case under older and looser forms of organization. In these circumstances it is inevitable that the stateman should calculate with increasing care the probable consequences of his acts, and that he should thus find himself forced into the position of requiring the aid of theories enabling him to predict as closely as possible the results which will flow from any course of action he may propose or adopt. Like the soldier, he realizes that his decisions may lead not merely to some form of personal failure but also to a disaster involving the entire society which he serves and guides. Accordingly, he is inclined to look favorably on the means which will help him to avoid the dangers and the pitfalls which lie ahead. Such an emphasis upon prediction as an increasingly important element in statecraft inevitably links statecraft with science, for the true distinction between science and other forms of organized knowledge lies in the concern of science with the possibility of accurate prediction. In so far as the statesman attempts to organize the knowledge relevant to his particular tasks in such a manner that he will be able to forecast the trend of events with an accuracy sufficient for his needs, he adopts the scientific attitude and gives science itself new scope.

My argument has now been developed to the point where it is necessary to weigh an objection frequently raised against attempts to consider history or politics in a scientific spirit. It is alleged that human affairs are essentially unpredictable and beyond the reach of experiment, thus falling outside the scope of scientific inquiry. I would contend that the experience of the war years does, in fact, run strongly counter to this allegation. Be that as it may, there is also room for rebuttal on logical grounds. An analysis of the objection as it is usually elaborated will show that it reposes essentially upon certain misunderstandings of the nature of modern science and, in particular, of scientific method. The science which, in this objection, is declared incommensurable with the essential character of history or politics proves upon examination to be that perfectly deterministic science with unrestricted capabilities of experimentation which constituted the philosophical ideal of the 18th and 19th Centuries and which reached its most complete expression in classical physics. It is well known, if not adequally appreciated, by everyone who discusses science that since 1900 physics has been subjected to a radical revision reaching down to its most fundamental principles. As a result it has to be conceded that, in principle as well as in practice, (1) it is not possible to know at a given instant of time all the factors which will prove to be relevant to events observable at a specified subsequent instant; (2) it is necessary to place all predictions on a statistical basis, at a sacrifice of determinism of the classical variety; and (3) it is impossible to conduct an experiment in which the experimental process does not influence in some measure the phenomena to be observed, altogether contrary to the convenient fiction that the system to be observed can be absolutely isolated from the rest of the universe throughout the experimental period.

In the case of physics there were both technical and psychological reasons why concessions along these lines were difficult to make, but in other branches of science, such as biology, psychology, and meteorology, they appear to be natural and obvious. Thus, it seems to me that, except for a matter of degree, we find science proceeding in its various recognized branches along the very lines which the skeptics consider inaccessible for the scientific method as soon as its application to history or politics is suggested. I am glad to say that the illogic of the skeptical position is beginning to be appreciated by workers in the field of social studies. As an instance, I might cite the lengthy discussion offered by Morgenthau under the title *Scientific man vs. power politics*.

A second objection to the extension of scientific method into the domain of social thought is more clearly of psychological origin and has, accordingly, less substance. This takes the form of characterizing all existing techniques as inadequate and simultaneously rejecting all innovations as speculative or unsound. There cannot be any logical answer to an objection of this order, but it might be worth pointing out that the techniques suitable to a particular field have been developed in the course of actual investigations quite as often as by transfer from other fields. It seems to me that the social sciences will have to devise many scientific techniques of their own in addition to those which can be borrowed from the more fully developed branches of science. On this point it is instructive to examine the very interesting approach to the mathematics of competition outlined by Von Neumann and Morgenstern in their recent book, *The theory of games and economic behavior*. To my mind their contribution illustrates very significantly the possibilities of designing new methods appropriate for the theoretical treatment of social phenomena at a scientific level.

Coming to the final stage of my argument, I should like to present the hypothesis that the moment is ripe for statecraft to draw enrichment on both the practical and the theoretical sides from contact with the spirit of science, and on this hypothesis, to discuss some of the developments which seem to me to be implicit in it.

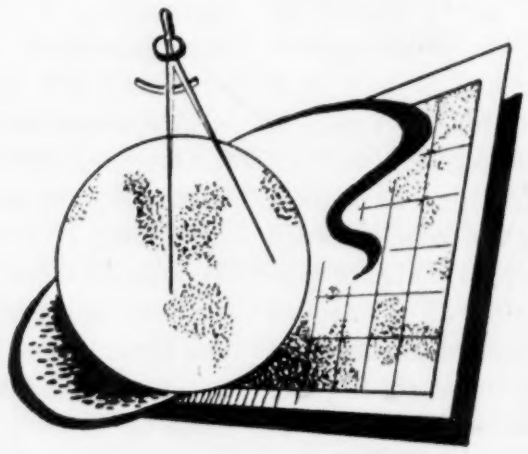
On the theoretical side I would anticipate that the demands of statecraft would greatly accelerate the introduction of scientific method into the social studies. It is quite clear, I think, that, once the social studies truly commit themselves in accord with the exigencies of our times to a serious attempt at prediction in the field of social phenomena, they will incline to loosen their ties with the fields of belles-lettres and moral philosophy—to their own considerable advantage.

On the practical side there should be greatly enlarged opportunities for the testing and revision of social and

economic theories, with extremely beneficial results for both the pure and the applied branches of social science. Social scientists have certainly been at a very great disadvantage in finding themselves too generally cut off from direct experience with statecraft and deprived of the means for checking such applications as may have been made of their theoretical contributions. During recent times, when a marked modification in this state of affairs has been quite evident, many theorists have seemingly used their opportunities primarily to put their theories into practice in a reformist and somewhat doctrinaire spirit, without any real interest in the actual as opposed to the fancied consequences of so doing. If I am right in thinking that the potentialities of disaster are slowly forcing statesmen to a much more careful reckoning of the consequences of their acts, then I would anticipate that in the future both theory and practice in the social studies would assume a character considerably more objective than this and more nearly consonant with their claims to rank as branches of science. I would expect that this practical influence would prove more potent than any purely philosophical arguments concerning the essentially scientific nature of the social studies; in referring to it earlier in its military aspects and in now mentioning it again, I stress the likelihood that this influence will indeed be a profound one.

The problem of matching theory and practice is difficult, even in the fields of physics and engineering, and becomes formidably so in the domain of statecraft. In general, this problem has been badly neglected in the past, apparently on the assumption that any clearly stated theory would somehow be reduced by practical men to practical utility without the intervention of any agency specifically designed to facilitate and accelerate the process. During the war, however, a great deal of experience in the conduct of highly technical military operations has shown that a rapid adjustment between theory and practice, such as was desperately needed in many situations, can best be attained by organizing teams to work specifically and directly with this kind of problem. Something of the same kind must be done, I think, in the domain of statecraft, if theory and practice are to be brought successfully together. At best, scientific theories uniformly present a rather fragmentary and somewhat idealized synthesis which provides only a more or less approximate understanding of any specific concrete problem; and this is particularly obvious in the case of the social sciences, dealing as they do with the most complex phenomena of all. It thus appears to be in the nature of things that there should be created a new art devoted to the skillful interweaving of theoretical insights with practical experience in a variety of domains, including that of statecraft.

In conclusion, I should like to mention a concrete problem upon which the scientist and the statesman have already begun to collaborate. This is the problem of understanding and controlling the impact upon society of the discoveries made in the physical and biological sciences. The recently formed Atomic Energy Commission is, no doubt, primarily intended to provide for a properly safeguarded engineering development of atomic power, but it will obviously have to consider many questions which fall within the domain of the social sciences. It seems to me important that similar attention should be given to the social effects of the many other innovations flowing in an ever-widening stream from our laboratories. Some of the proposals for a National Science Foundation contemplate the creation of a branch or section of the Foundation which should be devoted to work in the social sciences. I should like to suggest that such a branch could most fruitfully concentrate its attention and resources upon the problems to which I have just alluded. It seems clear that successful scientific work on this problem is not beyond our present capabilities and would go a long way toward laying the foundations for that broad and intimate union of science and statecraft which, in my opinion, must ultimately be formed.



Effects of an Antibiotic From *Aspergillus fumigatus* Fresenius on Tumor Cells *in Vitro*, and Its Possible Identity With Gliotoxin

John G. Kidd[1]

Department of Pathology, Cornell University Medical College,
and *The New York Hospital, New York City*

IN SPITE OF THE DIFFICULTIES NOW INherent in the supposition that a chemotherapeutic agent can be found which will act against cancer cells without harming their normal prototypes, much research has been directed toward this end in recent times. Detailed studies already completed in this laboratory have made it plain that the growth of Brown-Pearce rabbit carcinoma cells can be suppressed under a variety of experimental conditions by an antibody that reacts specifically with a distinctive constituent of the tumor cells but not with similar constituents of other rabbit cells, either normal or neoplastic (*5*, *6*). Subsequent work extending over a period of several years has shown that a mold, isolated originally from the air of an animal room and later identified as *Aspergillus fumigatus* Fresenius, provides culture filtrates that will regularly render the cells of various animal tumors incapable of further proliferation upon brief contact with them *in vitro*. Recently a crystalline substance identical with, or similar to, gliotoxin[2] has been isolated from the culture filtrates. Both this material and purified gliotoxin procured from another source have likewise proved highly active against tumor cells *in vitro*.

Effects of Culture Filtrates on the Cells of Various Animal Tumors

Following growth of the mold (designated A21 in our laboratory) on the surface of a modified Czapek-Dox medium in Blake bottles for 7–12 days at 28°–30°C., the culture liquids, which generally have a pH in the neighborhood of 3.5–4.5, are filtered through paper and stored in the refrigerator. To test for effects upon tumor cells, the culture filtrates are brought to a pH of 7.4 with NaOH, appropriately diluted with buffered Ringer's solution (pH 7.4) containing 250 mg. per cent of glucose, and incubated 2 hours at 37°C. with suspensions in the same medium of one or another of three types of tumor cells—a lymphosarcoma of C_3H mice (Gardner tumor), a sarcoma (RSI), and the Brown-Pearce carcinoma of rabbits.

Dilutions of the culture filtrates from 1:10 to 1:80 have usually prevented entirely the growth of the tumor cells upon implantation of the mixtures in suitable situations in susceptible hosts following the 2-hour sojourn *in vitro*; under these circumstances, dilutions of 1:160 and more have often affected the cells so that only small growths resulted, while control suspensions of the tumor cells in buffered glucose-Ringer's, incubated concurrently, have always given rise to large growths when implanted in corresponding situations in the same test animals. Later experiments have shown that incubation *in vitro* is unnecessary, the tumor cells being inhibited by a few minutes contact with potent culture filtrates at room temperature. The presence of broth or of serum has not diminished the tumor-inhibiting potency of culture filtrates.

Another strain of *A. fumigatus* Fresenius, procured from a different source and designated HA in our laboratory, although resembling A21 in appearance and being somewhat similar to it in cultural characteristics, has provided culture filtrates with comparatively little or no activity against tumor cells; the same has proved true of a variety of other molds.

Characteristics and Effects of an Antibiotic Substance Isolated From the Culture Filtrates

The A21 culture liquids have retained their activity apparently undiminished for several months when kept in the acid state in the refrigerator. When shaken with chloroform, the tumor-inhibiting substance has gone into the organic solvent, the remaining watery solution being devoid of inhibitory ability, while the chloroform extracts, evaporated to dryness, have yielded a gummy substance (about 0.1 mg. from each cubic centimeter of the original metabolite solution) which, redissolved in a small amount of alcohol and diluted appropriately with buffered glucose-Ringer's, has been quite as potent against tumor cells as was the original material.

As a first step toward learning whether the active material produced by *A. fumigatus* Fresenius (A21) might

[1] These investigations have been aided by a grant from the Jane Coffin Childs Memorial Fund for Medical Research. It is a pleasure to acknowledge the able assistance of Miss Rose Robbins in the work.

[2] Gliotoxin is a sulfur-containing compound for which an unusual structure and the formula $C_{13}H_{14}O_4N_2S_2$ have been suggested (*1*, *2*, *4*); it was first isolated as a product of *Gliocladium fimbriatum* by Weindling and Emerson (*9*) and is prominent among the antibiotic substances produced by molds of the genus *Aspergillus* (*3*, *7*, *8*).

be similar to gliotoxin, tests were made of the effects of heat upon it, for it is known that gliotoxin is remarkably unstable when heated in alkaline solution (*7*, *9*). In two experiments it was found that culture filtrates having pH levels of 3.58 and 3.64, respectively, placed in a boiling water bath for 10 minutes and brought to pH 7.8 after cooling, were quite as potent against Gardner lymphosarcoma cells as were unheated specimens that had been adjusted to pH 7.8 and allowed to stand meanwhile at room temperature, all being inhibitory in every dilution up to and including 1:160; the same filtrates, however, brought to pH 7.8 and then heated at 100°C. for 10 minutes, smelled strongly of hydrogen sulfide and subsequently were found to have lost all demonstrable activity against tumor cells. It is noteworthy in this relation that a similar amount of heating in an alkaline medium inactivated the gliotoxin or gliotoxin-like compound produced by the strain of *A. fumigatus* employed by Menzel, Wintersteiner, and Hoogerheide (*7*).

A sample of purified gliotoxin prepared by Johnson, Bruce, and Dutcher in the Baker Laboratory of Chemistry, Cornell University, and made available by Prof. du Vigneaud, was next tested for activity against tumor cells. In all concentrations of 1.0 μg./ml. and greater, this completely inhibited the growth of Gardner lymphosarcoma cells when incubated with them for 2 hours at 37°C.; dilutions containing 0.1 μg./ml. and less were not notably effective.

As a further step in identifying the active substance, a small amount of crystalline material was isolated from an A21 culture filtrate by the method of Menzel, Wintersteiner, and Hoogerheide (*7*); this proved indistinguishable under the microscope from the reference sample of purified gliotoxin.[3] When dissolved in buffered glucose-Ringer's solution it proved to be about as active against Brown-Pearce carcinoma cells as was the known gliotoxin, both materials in concentrations of 5 μg. and more/ml. preventing completely or almost completely the subsequent growth of the carcinoma cells held in contact with them for 2 hours at 37°C. Neither was active against these cells, however, in concentrations of 1 μg. and less/ml. Both the A21 crystalline material and the purified gliotoxin smelled strongly of hydrogen sulfide when saturated solutions of them at pH 7.4 (containing less than 200 μg./ml.) were placed in a boiling water bath for 10 minutes, and both of the heated specimens proved devoid of activity when tested subsequently against Brown-Pearce carcinoma cells.

[3] The writer is indebted to Prof. du Vigneaud for advice and suggestions concerning the characterization of the crystalline material, and to Dr. Rachele for confirming the observation on the similarity of the isolated crystals and those of the purified gliotoxin. Dr. Melville generously determined the melting points on the crystalline A21 material and the sample of purified gliotoxin and also interpreted ultraviolet absorption curves on both. He reports that the micro melting points and a mixed micro melting point were not inconsistent with the possible identity of the sample of gliotoxin and that of the isolated compound, though the melting points were spread over a range of several degrees in all three cases. The ultraviolet absorption curves on both samples were quite similar to the published curves for gliotoxin.

Further Tests With the Antiobiotic and With Various Types of Cells

Culture filtrates having notable potency against tumor cells *in vitro* exhibited no activity against *Treponema pallidum*, *Plasmodium lophurae*, or *Trypanosoma lewisi* in a variety of similar tests, and they failed to inhibit growth in broth of a variety of microbes, including staphylococci, streptococci, pneumococci, meningococci, and *Escherichia coli*. They did not diminish the motility of human spermatozoa, as tested by John MacLeod, and had no influence on the ciliary movement of rabbit tracheal epithelium upon prolonged contact therewith *in vitro*, although the ciliary beating ceased abruptly upon contact with anisotonic solutions, fixatives, acids, and alkalis. Solutions containing large amounts of the tumor-inhibiting antibiotic did not bring about lysis of sheep's erythrocytes in 2 hours at 37°C., although they caused inflammation and necrosis in the skin and subcutaneous tissues of mice and rabbits—the effects being roughly proportional to their tumor-inhibiting potency—and they proved lethal to mice when injected in sufficient amounts.

Tumor cells of the three types employed in the present study, incubated for periods of 4–5 hours with excessive amounts of potent culture filtrates, have, upon scrutiny under the microscope, looked precisely like those incubated concurrently with buffered glucose-Ringer's solution, as repeated examinations have shown; this proved true also in the case of Brown-Pearce carcinoma cells that had undergone prolonged incubation with saturated solutions of the A21 crystalline material and of the purified gliotoxin before examination with the phase microscope by Hans Zollinger. The latter observation would seem to have added significance when contrasted with the fact, recently studied in this laboratory by Dr. Zollinger, that normal and neoplastic cells "killed" by fixatives, heat, molar NaCl, surface-active agents, etc. immediately manifest irreversible morphological changes that prove readily visible with the phase objective.

In an experiment to determine whether the activity of culture filtrates against tumor cells ***in vitro*** could be altered, perhaps differentially, by prior incubation with suspensions of various tissue cells, two culture filtrates were incubated 4 hours at 37°C. with suspensions of citrated mouse blood and with suspensions of washed mouse liver, spleen, kidney, and Gardner lymphosarcoma cells. The incubated mixtures were then centrifuged and the supernatant liquids tested in the usual way for activity against fresh Gardner lymphosarcoma cells. The various suspensions had not discernibly affected the more potent of the two filtrates, all of the incubated aliquots of this material inhibiting completely in the two dilutions tested (1:10 and 1:40) the subsequent growth

of the fresh lymphosarcoma cells with which they were held in contact during 2 hours at 37°C. The findings were otherwise, however, with the weaker of the two filtrates. The portion incubated with the suspension of Gardner lymphosarcoma cells was devoid of activity in the test with fresh tumor cells in dilutions of 1:10 and 1:40, and those portions incubated with citrated mouse blood and with washed mouse kidney remained inhibitory in the 1:10 but not in the 1:40 dilution; the aliquots incubated with suspensions of spleen and liver cells, by contrast, had retained much, and perhaps nearly all, of their tumor-inhibiting potency, being completely inhibitory in the 1:10 dilution and almost so at 1:40, although this potency was slightly diminished when compared with that of the control aliquot that had been incubated with Ringer's solution.

In manometric experiments performed by Dr. William H. Summerson it was found that anaerobic glycolysis proceeded equally in mixtures containing Gardner lymphosarcoma cells and (a) crystalline A21 material in saturated solution in buffered glucose-Ringer's, (b) gliotoxin, also in saturated solution in the same medium, (c) a potent culture filtrate in a dilution of 1:10, and (d) control buffered glucose-Ringer's solution. Further tests provided evidence that oxygen consumption and glycolysis under aerobic and anaerobic conditions of Gardner lymphosarcoma and Brown-Pearce carcinoma cells were not altered by the presence of amounts of an active culture filtrate more than sufficient, as subsidiary tests proved, to prevent subsequent growth of the cells.

Tests for Chemotherapeutic Activity

Tests for *in vivo* activity against tumor cells with whole filtrates and with chloroform extracts of them have not thus far yielded encouraging results. In one experiment, for example, a small "dose" of Gardner lymphosarcoma cells was injected intraperitoneally into five groups of C_3H mice, each containing four animals of uniform weight. Immediately afterward the mice of the control group were injected intraperitoneally with 1 ml. of buffered glucose-Ringer's solution, while each of the mice of the other four groups received 1 ml. of one or another of four potent culture filtrates that had been brought to pH 6.5–7.0, the amounts of the latter administered to each mouse being greatly in excess of what would have been required to inhibit the growth of the lymphosarcoma cells following *in vitro* contact. All of the mice developed intraperitoneal lymphosarcomata within 2 weeks, the growths appearing as promptly and growing as rapidly in the animals of the experimental groups as in the controls. In a number of other experiments, culture filtrates were administered repeatedly to C_3H mice in near-lethal doses, both before and after implantation of minimal effective numbers of lymphosarcoma cells; in no case has there been any evidence that the subsequent course of events was significantly altered by the injections. Chloroform extracts of the culture filtrates, evaporated to dryness and taken up in concentrated form in alcoholic and watery solutions, have also been administered repeatedly to mice in near-lethal amounts without influencing significantly the course of implanted lymphosarcoma cells. Toxicity tests have shown, however, that both the filtrates and the chloroform extracts contain toxic substances that produce effects distinct from those of the crystalline A21 material and of gliotoxin. Tests for *in vivo* activity against tumor cells will be undertaken with the crystalline A21 compound and with purified gliotoxin as soon as sufficient amounts of the materials can be procured.

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Electron Configurations of "Rare-Earth" Elements

William F. Meggers
National Bureau of Standards, Washington, D. C.

THE DISCOVERY OF FISSION OF URANIUM atoms by Hahn and Strassmann in 1939 has led to the most spectacular scientific developments in the world's history. Direct consequences were atomic energy release by chain reactions, culminating in the atomic bomb of 1945, and neutron sources of fantastic intensity with which it has been possible to manufacture significant amounts of new elements and isotopes. The artificial elements of greatest interest are the transuranic elements, 93 (neptunium), 94 (plutonium), 95 (americium), and 96 (curium), since both theoretical calculations and chemical speculations have been made as to the probability of 5*f*-type electrons appearing in the 7th period of the Periodic Table. The purpose of the present discussion is to review some of these suggestions and to draw attention to the spectroscopic evidence bearing on this question.

In 1926 Sugiura and Urey (*6*), from quantum-theoretical calculations of central fields based on X-ray terms, were "led to the expectation that levels corresponding to the interior 5_4 electrons should not appear before an element with atomic number 95."

In 1933 Wu and Goudsmit (*7*) calculated from Schrödinger's equation the energies of various electrons of atoms and ions built upon the radon core and concluded that "beginning with element 93 we have to consider the sixfold ionized atom to obtain the ion with the radon core and in this ion the 5*f* is certainly the lowest level. This makes it very probable that the neutral atom 93 in its normal state contains at least one 5*f* electron."

In 1941 Mayer (*3*), from calculations of the eigen functions of the 4*f* and 5*f* electrons, concluded that "the calculations for the rare-earth group agree moderately well with experimental facts. The theory would predict that the 4*f* orbits start to be filled at Z = 61, or Z = 60, at the earliest. Actually the first 4*f* electron occurs at Z = 58. In the neighborhood of Z = 92 the theory predicts occurrence of a second rare-earth group; the first filled 5*f* level should occur at Z = 91 or 92. Experimentally it appears that uranium does not yet possess a 5*f* electron. Inaccuracies of a few units in Z are to be expected in a calculation based on the statistical model."

Quantum theory, wave mechanics, and quantum mechanics have thus far failed to yield an accurate solution of this problem.

In 1940 McMillan and Abelson (*2*) announced the discovery of radioactive element 93 and stated that "the new element has little if any resemblance to its homologue rhenium. This fact together with the great similarity to uranium suggests that there may be a second 'rare-earth' group of similar elements starting with uranium."

In 1946 Seaborg (*5*), after reviewing the oxidation states of the transuranic elements, said that "the evidence strongly indicates that we are dealing here with a transition series of elements in which the 5*f* electron shell is being filled in a manner similar to the filling of the 4*f* electron shell in the well-known rare-earth series. Apparently this new transition series begins with actinium in the same sense that the rare-earth series begins with lanthanum, and, although the first elements in the heavy series exhibit the property of undergoing oxidation to higher states up to a maximum oxidation state of VI, the tendency in the later members of the series is to have a stable lower oxidation state, such as the III state. The most important criterion for arranging the heavy elements in this series is the probable presence of seven 5*f* electrons (analogous to the stable gadolinium structure) in tripositive curium (element 96), rather than the presence of the first 5*f* electron in thorium. In fact, there might not be any such electrons in thorium with, for example, their first appearance in protoactinium (two 5*f* electrons) or in uranium (three 5*f* electrons); and, of course, it is recognized that the 5*f* and 6*d* shells of the elements in this region lie so close together that the energy necessary for the shift from one shell to the other may in some cases be within the range of chemical binding energies. Previous to the discovery of the transuranium elements, it was almost the universal attitude that a simple filling of the 6*d* shell of electrons was taking place (*i.e.* in the elements of atomic numbers 89–92), and practically all the standard works and textbooks on chemistry and physics adopted this view. It was possible to come definitely to this other view only as a result of the study of the transuranium elements. However, it should be pointed out that a number of people have previously made the suggestion that the 5*f* electron shell begins to be filled in this region, just before or after uranium. It is beyond the scope of the present discussion to review these suggestions."

The chemical evidence proves conclusively that elements 93, 94, 95, and 96 are not homologues, respectively, of elements 75 (rhenium), 76 (osmium), 77 (iridium), and 78 (platinum), but beyond this there is no chemical proof that the heaviest elements contain 5*f* electrons except by analogy with the rare earths 58 (cerium) to 64 (gadolinium), which are known from spectroscopic (not chemical) evidence to contain 4*f* electrons. Chemists usually include 21 (scandium), 39 (yttrium), and 57 (lanthanum)

in the rare earths because they exhibit similar properties (excepting spectroscopic) and oxidation states. Spectroscopists do not regard these three elements as true rare earths because they have no *f*-type electrons in their normal configurations. The valence electrons of these elements are d^1s^2 or d^2s^1. As a matter of fact, there is no direct chemical evidence for the existence of *f*-type electrons in any atoms. In the 4*f*-type rare earths (except 58 Ce) the 4*f* electrons are completely submerged in the N shell; they are inactive as valence bonds compared with the less firmly bound 5*d* electrons in the O shell or 6*s* electrons in the P shell. In the 5*f*-type rare earths the differences between binding forces on 5*f*, 6*d*, and 7*s* electrons are less, and again there is no chemical evidence for distinguishing between them. All that can be said is that, because 96 Cm in period 7 shows only tripositive valence, it may be assumed that some electrons (presumably 5*f*) are submerged and inactive, analogous to the inactive ones (4*f*) of 64 Gd in period 6. Chemical evidence, however, does not distinguish between $5f^76d^17s^2$ and $5f^16d^77s^2$, since it is well known that type 3*d*, 4*d*, and 5*d* electrons are generally also chemically inactive after their subgroups are half filled.

Spectroscopic evidence for distinguishing *d*- and *f*-type electrons is unique and unambiguous. There are two kinds of spectroscopic evidence: (1) absorption spectra of compounds in solution and (2) emission spectra of atoms or ions. The absorption spectra of certain compounds in solution are characterized by relatively narrow bands approaching in sharpness atomic spectrum lines. Such absorption bands have been reported for the elements 58 (cerium) to 70 (ytterbium), inclusive, and for 92 (uranium) but not for 21 (scandium), 39 (yttrium), 57 (lanthanum), or 90 (thorium). They have not been re-

TABLE 1

ELECTRON CONFIGURATIONS AND LOWEST TERMS OF "RARE-EARTH" SPECTRA

Atomic No.	Element	Theoretical (a)		Experimental							
				Neutral atoms		Singly ionized		Doubly ionized		Trebly ionized	
		Electrons	Terms	Electrons	Terms	Electrons	Terms	Electrons	Terms	Electrons	Terms
58	Ce	$4f^1\ 5d^1\ 6s^2$	$^3H°$	$(4f^2\ 6s^2)$	(^3H)	$4f^2\ 6s^1$	^4H(b)	$(4f^2)$	(^3H)(c)	$4f^1$	^2F(d)
59	Pr	$4f^2\ 5d^1\ 6s^2$	^4K	$(4f^3\ 6s^2)$	$(^4I°)$	$4f^3\ 6s^1$	$^5I°$(e)				
60	Nd	$4f^3\ 5d^1\ 6s^2$	$^5L°$	$4f^4\ 6s^2$	^5I(f)	$4f^4\ 6s^1$	^6I(g)				
61		$4f^4\ 5d^1\ 6s^2$	^6L	$(4f^5\ 6s^2)$	$(^6H°)$						
62	Sm	$4f^5\ 5d^1\ 6s^2$	$^7K°$	$4f^6\ 6s^2$	^7F(h)	$4f^6\ 6s^1$	^8F(i)				
63	Eu	$4f^6\ 5d^1\ 6s^2$	^8H	$4f^7\ 6s^2$	$^8S°$(j)	$4f^7\ 6s^1$	$^9S°$(k)	$4f^7$	$^8S°$(k)		
64	Gd	$4f^7\ 5d^1\ 6s^2$	$^9D°$	$4f^7\ 5d^1\ 6s^2$	$^9D°$(l)	$4f^7\ 5d^1\ 6s^1$	$^{10}D°$(m)				
65	Tb	$4f^8\ 5d^1\ 6s^2$	^8H	$(4f^9\ 6s^2)$	$(^6H°)$						
66	Dy	$4f^9\ 5d^1\ 6s^2$	$^7K°$	$(4f^{10}\ 6s^2)$	(^5I)						
67	Ho	$4f^{10}\ 5d^1\ 6s^2$	^6L	$(4f^{11}\ 6s^2)$	$(^4I°)$						
68	Er	$4f^{11}\ 5d^1\ 6s^2$	$^5L°$	$(4f^{12}\ 6s^2)$	(^3H)						
69	Tm	$4f^{12}\ 5d^1\ 6s^2$	^4K	$4f^{13}\ 6s^2$	$^2F°$(n)	$4f^{13}\ 6s^1$	$^3F°$(n)				
70	Yb	$4f^{13}\ 5d^1\ 6s^2$	$^3H°$	$4f^{14}\ 6s^2$	^1S(o)	$4f^{14}\ 6s^1$	^2S(o)				
71	Lu	$4f^{14}\ 5d^1\ 6s^2$	^2D	$4f^{14}\ 5d^1\ 6s^2$	^2D(p)	$4f^{14}\ 6s^2$	^1S(p)	$4f^{14}\ 6s$	^2S(p)		
90	Th	$6d^2\ 7s^2$	^3F	$6d^2\ 7s^2$	^3F(q)	$6d^2\ 7s^1$	^4F(r)	$6d^2$	^3F(s)	$6d^1$	^2D(t)
91	Pa	$6d^3\ 7s^2$	^4F	$(5f^2\ 6d^1\ 7s^2)$	(^4K)	$(5f^2\ 7s^2)$	(^3H)				
92	U	$6d^5\ 7s^1$	^7S	$5f^3\ 6d^1\ 7s^2$	$^5L°$(u)	$5f^3\ 7s^2$	$^4I°$(f)				
93	Np			$(5f^4\ 6d^1\ 7s^2)$	(^6M)	$(5f^4\ 7s^2)$	(^5I)				
94	Pu			$(5f^5\ 6d^1\ 7s^2)$	$(^7K°)$	$(5f^5\ 7s^2)$	$(^6H°)$				
95	Am			$(5f^6\ 6d^1\ 7s^2)$	(^8H)	$(5f^6\ 7s^2)$	(^7F)				
96	Cm			$(5f^7\ 6d^1\ 7s^2)$	$(^9D°)$	$5f^7\ 7s^2$	$(^8S°)$				

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ported for transuranic elements, probably because such information is at present secret. It is assumed that these bands are associated with the presence of *f*-type electrons in these ions, but this evidence is inconclusive as to the exact nature or number of the electrons involved.

The only way to distinguish the different types of electron orbits and to determine how many of each are present in an atom or ion is by way of the characteristic emission spectrum. Experimental analyses of spectral structures, supported in most cases by the Zeeman effect, have revealed the true electronic structure of atoms. Being, in general, extremely complex, the spectra of rare earths have been the last to succumb to structural analysis. Some are only partially analyzed, and others are still untouched, but sufficient information is now at hand to justify its review in connection with the question under discussion. The results are summarized in Table 1, where small letters in parentheses (a, b, c, etc.) refer to publications cited in the table and other symbols in parentheses represent extrapolations or predictions based on the analyses of neighboring spectra. The extrapolations are made on the assumption that for the production of successive ions and spectra the principal ionization always occurs by removal of the least firmly bound electron without any change or redistribution of the remaining electrons. Thus, if the normal configuration of Ce II is $4f^26s^1$, it is predicted that the normal configuration of Ce I will be $4f^26s^2$, and not $4f^15d^16s^2$. This is not a universal rule, since, for example, the normal configurations of La I and La II are found to be $5d^16s^2$, and $5d^2$, respectively, but it is valid for all rare-earth spectra that have been analyzed.

In 1932 Russell and Meggers (*4*) identified in La I and La II spectra excited states due to configurations involving 4*f* electrons, called attention to the fact that the terms produced by the 4*f* electrons lie lower than those arising from the 6*p* electron, and stated that this is obviously related to the fact that 4*f* electrons are bound into the normal state of the directly following elements, 58 (cerium) to 71 (lutecium), while the 6*p* electrons begin to be similarly bound only in element 81 (thallium). If my prediction for Ce is correct, the normal configuration of $5d^16s^2$ for 57 La becomes $4f^26s^2$ for 58 Ce.

Long ago the spectral analyses of 4th period elements containing 3*d* electrons revealed that an extra electron is seized by the 4th atom (24, chromium) to half fill the group and again by the 9th (29, copper) to fill it completely. Spectral analyses of 5th-period elements also proved that in atomic accretion an extra 4*d* electron is seized by the 3rd (41, columbium) and following atoms and again by the 8th (46, palladium). In the 6th period a similar tendency prematurely to half fill or wholly fill the 4*f* shell was expected, but it was not known where these accelerated accessions would begin. Spectroscopic results now available indicate that an extra 4*f* electron most likely is acquired at the very beginning (58, Ce) and again immediately after the shell is half filled (65, terbium). The 4*f* subgroup is half filled in the 6th rare earth (63, europium) and completely filled in the 13th (70, ytterbium). These facts explain the occasional divalent character of 63 Eu and 70 Yb atoms and suggest that the common compounds in which all rare earths are trivalent involve excited states ($5d^16s^2$ or $5d^26s^1$) rather than ground states (except 64 Gd and 71 Lu).

The facts concerning 5*f* electrons in the 7th period appear to be somewhat different. According to present spectroscopic information no *f*-type electrons are present in the normal states of 90 Th atoms or ions. The normal state of Th IV is ascribed to $6d^1$, that of Th III to $6d^2$ (probably), that of Th II to $6d^27s^1$, and that of Th I to $6d^27s^2$ (probably). The best-analyzed spectrum of this group is Th II, in which excited states identified with 5*f* electrons begin 4,490 cm.$^{-1}$ above the ground level, thus anticipating the binding of such electrons in the normal structures of succeeding atoms. It appears very likely that two 5*f* electrons will be found in the normal configuration of element 91 (protoactinium), because reliable analyses of the first two spectra of 92 U have proved conclusively that these atoms and ions contain three 5*f* electrons as a minimum. The ground state of U II is $5f^3-7s^2$. Levels arising from $5f^36d^17s^1$ begin at 289 cm.$^{-1}$, and those arising from $5f^36d^2$ begin at 4,585 cm.$^{-1}$ Other energy levels found in the U II spectrum have been identified with the electron configurations $5f^47s^1$, and $5f^5$. The ground state of U I is $5f^36d^17s^2$, and levels from $5f^36d^27s^1$ begin at 6,249 cm.$^{-1}$ This spectroscopic answer to the 5*f* question is positive and decisive; it was made available to the Manhattan Project on February 7, 1944, and was released to the public by Kiess, Humphreys, and Laun (*1*) on March 9, 1946. The preferred oxidation state VI of 92 U is interpreted to mean that in this case three 5*f*, one (or two) 6*d*, and two (or one) 6*s* electrons contribute equally to valence bonds, and the gradual shift in preferred oxidation state to III with higher atomic numbers is simply explained by the increase in stability of the 5*f* group as this shell approaches a condition of being half filled, at which point it no longer participates in the formation of chemical compounds. Although the electron configurations of transuranic elements are predicted with considerable confidence, any opportunities for testing the predictions by direct spectroscopic observation and interpretation should not be neglected.

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NEWS *and Notes*

The unexpected addition of more than 2,100 new AAAS members between January 1 and May 1, 1947, has led to a shortage of copies of some issues of *Science* in the interval. The reason for this shortage is that each new member in the first six months of the year has been sent back issues of the journal of his choice.

Back issues of *Science* lacking at the moment are Nos. 2717 and 2718 (January 24 and 31), Nos. 2719, 2720, 2721, and 2722 (all February issues), and Nos. 2724 and 2725 (March 14 and 21). Receipt of copies of these issues from members who do not maintain permanent files will be greatly appreciated. They should be sent to: American Association for the Advancement of Science, 1515 Massachusetts Avenue, N. W., Washington 5, D. C. Postage will be refunded.

The British Association for the Advancement of Science, Burlington House, London W. 1, England, will hold its first full postwar annual meeting in Dundee, Scotland, August 27–September 3, 1947, under the presidency of Sir Henry Dale. The Council of the British Association will welcome representatives of the AAAS at the Dundee meeting. The last prewar meeting of the Association, held in Cambridge in 1938, was attended by more than 60 scientists from the United States.

Each of the 15 sections of the British Association has extended an invitation to an American scientist to attend. The Council of the British Association desires to learn the names of other American scientists who will be in England at the time of the meeting.

In 1938 the British Association and the AAAS entered into an arrangement for exchange lecturers on alternate years. At the Boston meeting C. B. Fawcett, of London University, delivered a lecture under this arrangement. The British will in turn invite an American scientist to lecture at the Dundee meeting.

Heavy water and deuterium gas are now being made available by the U.S. Atomic Energy Commission for research purposes within the United States. The abundance of the heavy hydrogen isotope in the material is approximately 99.9 per cent. Quantities will be limited to normal research requirements.

The Stuart Oxygen Company, San Francisco, California, will act as contracting agent for distribution. This company began small-scale production and distribution soon after the discovery of deuterium. In the postwar period, because of the increased need for deuterium in research, the Stuart Company's production has been far below the demand. The quantities being made available are from stock produced by other operators during the war for the Manhattan District.

The material will be distributed with charges based on the cost of handling and distribution. The cost of production of the material itself will not be included. Distribution in this manner is being effected under authority of the Atomic Energy Act of 1946, which provides for the fostering and assistance of research by the Commission.

Allocation will be handled in a manner similar to that for radioisotopes. For complete information write to: U. S. Atomic Energy Commission, Research Division, Field Operations, Oak Ridge, Tennessee. Attention: Isotopes Branch.

About People

Theodore G. Bernthal, formerly associate professor of physiology, Vanderbilt University School of Medicine, is now professor and head, Department of Physiology, Medical College of the State of South Carolina, Charleston.

John S. Karling, Columbia University, has been appointed visiting professor of mycology at Louisiana State University, Baton Rouge, for the 1947 summer term.

Frank Glenn, of The New York Hospital-Cornell Medical Center, has been appointed surgeon-in-chief of the Hospital and Lewis Atterbury Stimson professor of surgery at Cornell University Medical College, succeeding George J. Heuer, who will retire on July 1.

John Q. Griffith, Jr., director, Laboratory for the Study of Hypertension, Hospital of the University of Pennsylvania, will deliver the William Hamlin Wilder Memorial Lecture of the Institute of Medicine of Chicago May 23 at the Palmer House. Dr. Griffith's subject will be "Rutin: A Therapy for the Hemorrhagic Complications of Hypertension."

Sidney Howe Yarnell, formerly chief of the Division of Horticulture, Texas Agricultural Experiment Station, will join the staff of the U. S. Regional Vegetable Breeding Laboratory, Charleston, South Carolina, on June 1 as senior geneticist.

Charles A. R. Connor, New York University College of Medicine, has been appointed associate medical director of the American Heart Association.

Morris B. Jacobs has been appointed chief organic chemist, Research Laboratories, Bureau of Laboratories, Department of Health, City of New York.

Julian S. Schwinger, Harvard University, has been appointed full professor of physics, effective July 1. With his appointment at the age of 29, Dr. Schwinger becomes one of the youngest full professors in the history of the University. Dr. Schwinger has made many important contributions to the field in his work on the scattering of neutrons by ortho- and para-hydrogen, photodisintegration of the deuteron, the theory of wave guides, and the tensor theory of nuclear forces.

H. L. Haller, organic chemist with the Department of Agriculture, has been appointed special assistant to P. N. Annand, chief of the Bureau of Entomology and Plant Quarantine of the Department. The appointment became effective March 13. With L. B. LaForge and L. E. Smith, Dr. Haller determined the chemical structure of rotenone, an important organic insecticide, for which he and Dr. LaForge received the Hillebrand Prize of the Washington Chemical Society in 1932.

Selman A. Waksman will be guest speaker at the Initiation Banquet meeting of the Connecticut Chapter of the Society of the Sigma Xi at Storrs on May 22.

William S. Helt has joined the staff of the Department of Fish and Game, Texas A & M College, to assume charge of the ornithological work of the Department.

Visitors to U. S.

A. J. Amos, British authority on cereal chemistry, will address the convention of the American Association of Cereal Chemists at the Hotel President, Kansas City, on May 19. With Dr. Kent-Jones, Dr. Amos co-authored *Modern cereal chemistry*, recognized as classical in its field. Dr. Amos is at present actively engaged in studying the chemical determination of riboflavin and nicotinic acid under a program sponsored by the Society of Public Analysts and Other Analytical Chemists.

Henri Makower, director of the Institute of Microbiology, University of Wroclaw, Poland, spent several weeks in April at the University of Texas Medical Branch, Galveston, surveying studies of Ludwik Anigstein on the chemotherapy of rickettsial diseases and of Morris Pollard on virus diseases. Dr. Makower is visiting U. S. medical centers as a guest of the Rockefeller Foundation.

Grants and Awards

Ross G. Harrison, professor emeritus, Osborn Zoological Laboratory, Yale University, was presented the John J. Carty gold medal and award for 1947 at the annual dinner of the National Academy of Sciences in Washington, D. C., April 29. Dr. Harrison received the award for his discovery that tissue cells may be grown outside the animal body, by which method he was able to demonstrate the manner of growth of nerve fibers; for his contributions as an investigator, teacher, and councilor of of students; and for his distinguished direction of the National Research Council from 1938 to June 1946.

F. A. Vening Meinesz, Dutch geodesist and geophysicist, is the recipient of the William Bowie Medal of the American Geophysical Union. The award was made at the closing session of the Union on April 30 at the Carnegie Institution of Washington, and accepted by H. Helb, of the Netherlands Embassy. Dr. Meinesz was the discoverer of a linear belt of negative gravity anomalies in the East Indies and interpreted these in relation to the structure of the earth. He has also greatly advanced the technique for observing gravitational anomalies, especially by the use of submarines.

George Howard Parker, emeritus professor of zoology, Harvard University, was elected to honorary membership in the Royal Zoological Society of Belgium on January 29.

Samuel Karlen, recent recipient of the Ph.D. degree in mathematics from Princeton University, has been appointed to the Harry Bateman Research Fellowship in pure mathematics by the Board of Trustees of California Institute of Technology. He will join the Mathematics Department of the Institute as a research fellow in September 1947.

The Bateman Fellowship, established this year by the Institute in honor of the late Harry Bateman, professor of mathematics, physics, and aeronautics, is awarded for one year but may be renewed for a second year. Dr. Karlen is the first to receive the appointment.

The California Institute of Technology, Division of Biology, has received from the Herman Frasch Foundation an annual grant of $10,000, renewable each year for a period of five years, for basic research in enzyme and protein chemistry in plant growth and development.

The Institute has conducted research in this field for the past 16 years. It will now undertake separation, isolation, and study of particular enzyme systems of higher plants, especially those having greatest interest in relation to plant growth.

The Loubat Prizes of $1,000 and $400, awarded every fifth year at the commencement exercises of Columbia University, are to be given again in 1948 for the best work printed and published in the English language on the history, geography, archaeology, ethnology, philology, or numismatics of North America. To be considered for the 1948 award, books must be published before January 1, 1948 and be submitted to the Secretary of Columbia University before February 1, 1948. The submitted material will be judged by John K. Wright, American Geographical Society; Leslie Spier, University of New Mexico; and Dexter Perkins, University of Rochester.

Northwestern University Medical School has received a gift of $50,000 from the James Foundation of New York, Inc., for use in its Institute for the Study of Rheumatic Fever, which is directed by Alvin F. Coburn. Research will be conducted in bacteriology, immunology, pathology, physiology, biochemistry, immunochemistry, enzyme chemistry, and possibly organic chemistry. In addition to fundamental research work, the Institute plans to engage in clinical research through collaboration with hospitals for the care of rheumatic children. Full-scale work will be initiated this summer.

Fellowships

The International Union of Biological Sciences invites applications for the following fellowships (1947): two at the Zoological Station, Naples, Italy; one at the Marine Biological Station, Roscoff, France; and one at the Central Bureau for the Cultivation of Fungi, Baarn, The Netherlands. These UNESCO/IUBS fellowships are open to graduated students of biology in its widest sense from universities all over the world. The value of each will be $750 (U. S. currency) for students from Europe and $1,000 (U. S. currency) for students from outside Europe (travel and lodging expenses included.) Applications, stating qualifications and experience and giving full information concerning the researches to be made, accompanied by two letters of recommendation by qualified biologists and, if available, one copy of earlier publications, should reach the Executive Committee of the International Union of Biological Sciences, % Prof. Dr. M. J. Sirks, Genetisch Instituut, Huis de Wolf, Haren, Groningen, The Netherlands, before October 1, 1947.

The Graduate Division of Conservation, Vassar College, is offering two fellowships for study in basic scientific problems relative to plants in the field of conservation leading to a M.S. degree in plant science. Further details may be obtained from Edith A. Roberts, Chairman, Department of Plant Science, Vassar College, Poughkeepsie, New York.

The Institute of Neurology, Northwestern University Medical School, announces the availability of fellowships for research in neuroanatomy and neuro-

physiology leading to the Ph.D. degree for candidates with Bachelors' degrees who intend to pursue an academic or research career in anatomy, physiology, or neurology. Applications should be made to the Director, Institute of Neurology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago 11, Illinois.

Colleges and Universities

The Ohio State University will make major changes in its Bachelor of Arts curriculum effective with the fall term. The program, which will allow almost no elective courses in the first two years of study, has been designed to give students a much broader background of general knowledge. According to Harlan Hatcher, dean of the College of Arts and Sciences, the program will require that each student acquaint himself with the methods and problems faced by the physical scientist, that special training be provided in the field of biological sciences, and that greater emphasis be placed upon the social sciences.

The Howard University Sigma Xi Club was recently installed in Washington, D. C., by Harlow Shapley, national president of Sigma Xi. The chapter has a charter membership of 18 members and two associate members. After the ceremonies, Dr. Shapley talked briefly of his recent visits to Russia and India and joined members in an informal discussion of astronomy, international relations, and the future of science.

Members of the Committee on Arrangements were: W. Montague Cogg, professor of anatomy; S. R. Cooper, professor of analytical chemistry; Walter T. Daniel, associate professor of mechanical engineering; Arthur H. Webb, instructor in bacteriology; and Herman Branson, professor of physics, chairman. Charles H. Thompson, dean of the Graduate School, represented the University.

The Bureau of Biological Research, Rutgers University, has announced that its program of studies of protein metabolism has received increased support from the University, the Quartermaster Corps of the Army, the Office of Naval Research, and some 13 industrial research laboratories.

New laboratories provided include air-conditioned animal rooms, a diet kitchen and physiological laboratories, and a large analytical laboratory. The program, under the direction of James B. Allison, of the University, investigates: the nitrogen balance indexes and, where possible, the sulfur balance indexes of proteins, polypeptides, and amino acids fed orally and intravenously to normal and protein-depleted animals; the effects of depletion and repletion in proteins on the physiological state of the animal and on the formation of plasma proteins, including antibodies to specific antigens; comparative antigenicity of proteins under a variety of experimental conditions; and the mutually dependent effects of protein depletion and endocrine imbalances on nitrogen and sulfur metabolism.

Summer Programs

A Statistical Summer Session will be held August 5–September 5 at the Virginia Polytechnic Institute, Blacksburg, under the joint sponsorship of the Institute, the University of North Carolina, University of Michigan, Iowa State College, and the Federal Bureau of Agricultural Economics. Courses will be offered for credit in: engineering statistics, statistical methods, design of animal experiments, schedule design and interview techniques for sample surveys, sampling design and analysis, mathematical theory of sampling, seminar, mathematical statistics, and experimental design. The faculty, which will be drawn chiefly from the cooperating organizations, will consist of: Rensis Likert, H. L. Lucas, Maurice G. Kendall and Frank Yates (England), George W. Snedecor, Earl E. Houseman, Raymond J. Jessen, and Boyd Harshbarger.

Inquiries regarding the session should be addressed to Boyd Harshbarger, professor of statistics, Virginia Polytechnic Institute, Blacksburg, Virginia.

Meetings

The Eastern Association of Electroencephalographers will hear three papers at its annual meeting on May 24 at the New York Hospital: "Place of Electroencephalography in the Psychiatric Hospital," W. T. Liberson; "The Electroencephalogram in Behavior Problems," Margaret Kennard; and "Electroencephalography in Psychopathic Personalities," D. J. Simons. During the morning the group will be invited to inspect the laboratories and facilities of the Hospital.

The American Heart Association, Inc., will hold its annual meeting at the Hotel President, Atlantic City, New Jersey, June 6–8, just prior to the meetings of the American Medical Association. The scientific sessions, on June 6 and 7, will be open to members of the medical profession and other interested persons.

The Engineering College Research Council will meet in Minneapolis, Minnesota, June 17–21, in connection with the American Society for Engineering Education meetings. In addition to Council affairs, there will be a symposium on "Relation of College Research Organizations to Industry," J. E. Hobson, Armour Research Foundation, presiding; a round-table discussion on "Research in Engineering Colleges Is a National Asset," C. A. MacQuigg, vice-president, presiding; and a joint meeting with the Electrical Engineering Division of the American Society for Engineering Education which will feature papers by F. E. Terman, Stanford University; J. R. Killian, Massachusetts Institute of Technology, and J. E. Hobson.

A symposium on the biological applications of isotopes will be sponsored by the University of Wisconsin, Madison, September 10–13. The program, which has been planned to include all phases of isotope work as it applies to the fields of biochemistry, physiology, bacteriology, plant physiology, and clinical medicine, will include papers by: A. Baird Hastings, Harvard Medical School; Harold C. Urey, University of Chicago; Glenn T. Seaborg, University of California; Paul C. Aebersold, Atomic Energy Commission, Oak Ridge, Tennessee; Alfred O. Nier, University of Minnesota; C. C. Coryell, Massachusetts Institute of Technology, and Martin Kamen, Washington University; Donald C. Melville, Cornell Medical School; David B. Sprinson, Columbia University; Harland G. Wood, Western Reserve University; Konrad Bloch, University of Chicago; David M. Greenberg, University of California; I. L. Chaikoff, University of California; Joseph G. Hamilton, University of California; Byron Hall, Mayo Clinic; Saul Hertz, Massachusetts General Hospital; and W. F. Bale, University of Rochester. In addition, there will be five panel discussions on various aspects of the subject.

Reservations and additional information may be obtained from E. C. Al-

bright, Department of Medicine, 1300 University Avenue, Madison 6, Wisconsin.

A Guidance Conference on the Measurement of Student Adjustment and Achievement, conducted by the Bureau of Psychological Services, will be held June 26–27 in Ann Arbor, Michigan, according to an announcement by the University of Michigan Institute for Human Adjustment. Leaders in the fields of psychology, education, and student personnel will present and evaluate recent researches and their practical application. Sessions of the conference will be devoted to several phases of the measurement of adjustment, the measurement of achievement, the prediction of academic success, and research problems for the future.

Those interested in attending the Conference may obtain complete information from Dr. Wilma T. Donahue, Bureau of Psychological Services, 1027 East Hurton Street, Ann Arbor, Michigan.

The National Conference on Industrial Hydraulics (formerly the Hydraulic Machinery Conference) will hold its third annual meeting October 16–17 at the Hotel Continental, Chicago. The subjects of the four half-day sessions will be: "Cavitation," "Industrial Application of Hydraulics," "Automotive Fluid Transmissions," and "Hydraulic Controls." The Conference is sponsored by Armour Research Foundation and the Graduate School of Illinois Institute of Technology, in cooperation with the Western Society of Engineers and the Chicago sections of the Society of Automotive Engineers, American Society of Civil Engineers, and the American Society of Mechanical Engineers.

Additional information may be obtained from Dr. V. L. Streeter, Armour Research Foundation, Technology Center, Chicago 16.

Elections

The Rockefeller Foundation has announced the election of the following as trustees: John Sloan Dickey, president of Dartmouth College; Robert F. Loeb, Lambert professor of medicine, Columbia University; and Henry Pitney Van Dusen, president of the faculties of Union Theological Seminary and Auburn Theological Seminary.

The Corrosion Division of the Electrochemical Society elected the following officers at its April meeting in Louisville, Kentucky: Hugh J. MacDonald, Illinois Institute of Technology, chairman; M. G. Fontana, Ohio State University, vice-chairman; and I. A. Denison, National Bureau of Standards, secretary-treasurer.

The Association of Southeastern Biologists, meeting with the Southeastern Section of the Botanical Society of America and the Southern Appalachian Botanical Club at Emory University on April 18–19, elected the following officers for 1947–48: Martin D. Young, U. S. Public Health Service, president; Samuel L. Meyer, University of Tennessee, president-elect; Howard M. Phillips, Emory University, vice-president; Elon E. Byrd, University of Georgia, secretary-treasurer; and Bruce D. Reynolds, University of Virginia, E. Ruffin Jones, Jr., University of Florida, and Frederick T. Wolf, Vanderbilt University, new members of the Executive Committee. A total of 44 papers, including 13 papers in a symposium on "Biological Stations in the Southeast," were presented during the meetings.

The 1948 meeting will be held at the University of Florida, Gainesville, April 16–17.

The American Geophysical Union, meeting in Washington, D. C., April 28–30, elected the following officers to serve for three-year terms: J. A. Fleming, Carnegie Institution of Washington, honorary president; O. E. Meinzer, Washington, D. C., president; H. U. Sverdrup, Scripps Institution of Oceanography, vice-president; and K. Hilding Beij, National Bureau of Standards, general secretary.

The new Section presidents, vice-presidents, and secretaries, respectively, also elected for three years, are as follows: Geodesy—H. W. Hemple, H. H. Hess, and Frank L. Culley; Seismology—Frank Neumann, Perry Byerly, and Florence Robertson; Meteorology—Horace R. Byers, Benjamin Holzman, and Woodrow C. Jacobs; Terrestrial Magnetism and Electricity—Irwin Roman, J. W. Joyce, and David G. Knapp; Oceanography—George F. McEwen, Edward H. Smith, and Richard H. Fleming; Volcanology—Wilbur S. Burbank, William F. Foshag, and Francis G. Wells; Hydrology—Lorenz G. Straub, F. J. Veihmeyer, and Ray K. Linsley, Jr.; Tectonophysics—M. King Hubbert, Robert Balk, and Wilbur S. Burbank.

The Southeastern Section of the American Physical Society has elected the following officers for 1947: Milton Braun, Cawtawba College, chairman; E. H. Dixon, University of Georgia, vice-chairman; Eric Rogers, University of Alabama, secretary; and H. F. Henry, University of Georgia, treasurer.

The New Orleans Academy of Sciences, at its 94th annual meeting held at Tulane University, New Orleans, Louisiana, on April 25–26, elected the following officers for 1947–48: Joseph Morris, Tulane University, president; Thomas T. Earle, Tulane University, vice-president; Walter G. Moore, Loyola University, secretary; J. Karlem Riess, Tulane University, treasurer; and Garland F. Taylor, Tulane University, curator.

The New York Pathological Society has elected Ludvig Hektoen, Pierre Masson, Peyton Rous, and Francis Carter Wood honorary members in recognition of their contributions to the science of pathology.

D. E. Jackson, professor of pharmacology, University of Cincinnati Medical College, Ohio, has been elected an honorary member of the Sociedad de la Farmacologia y Terapéutica de la Asociación Médica Argentina.

The South Carolina Academy of Science elected the following new officers for 1947 at its recent meeting in Columbia: Gilbert H. Collings, professor of agronomy and soils, Clemson College, president; J. T. Penney, University of South Carolina, vice-president; and Ralph E. Blakeley, Winthrop College, secretary-treasurer.

Recent Deaths

John Alden Loring, 76, field naturalist with the Theodore Roosevelt-Smithsonian scientific expedition to Africa in 1909 and onetime curator of animals at the New York and Denver Zoological Parks, died May 8 in Owego, New York.

Robert D. Evans, 54, consulting transmission engineer with the Westinghouse Electric Corporation since 1914, died May 8 at his home in Edgewood, Pennsylvania.

Cassius Jackson Keyser, 84, emeritus Adrain professor of mathematics at Columbia University, died May 8 at his home in New York City. Prof. Keyser had been associated with the University since 1897. The first volume of his hitherto unpublished essays, now being published by a group of his friends, was to have been presented to him on his birthday, May 15.

The AAF-National Geographic Society solar eclipse expedition (*Science*, January 3) will be complete with the arrival in Bocayuva, Brazil, of the C-54 which left National Airport, Washington, D. C., on May 10. Aboard the plane, along with newspapermen, photographers, and radiomen, were Lyman J. Briggs, chairman of the National Geographic Society's research committee; Martin A. Pomerantz, Bartol Research Foundation; and Irvine C. Gardner, National Bureau of Standards. NBC will broadcast a description of the eclipse, which will not be visible in the United States, at 8:30 A. M. (EDT) on May 20.

The American Midland Naturalist will be under the editorship of John D. Mizella, Department of Biology, University of Notre Dame, managing and associate editor of the journal since December 1946, upon the resignation of Theodor K. Just, chief curator, Department of Botany, Chicago Natural History Museum, effective with the completion of the current volume (37). Future communications in regard to manuscripts, subscriptions, exchanges, etc. should be addressed to Dr. Mizella at Notre Dame, Indiana.

The National Registry of Rare Chemicals, Armour Research Foundation, 35 West 33rd Street, Chicago 16, Illinois, lists the following wanted chemicals: trihexylamine, squalene, phytic acid, dimethyl tellurium, dimethyl cadmium, perparine, octaverin, anhydrotetronic acid, desoxyribose, ethyl boric acid, d-glucurone, angelic acid, sparassol, quercimeritrin, pellotine, cotarnine, citraconic acid, silver tetraborate, phosphopyruvic acid, and tetramethylene diisocyanate.

The British Department of Scientific & Industrial Research has appointed three new chairmen of the Department's Research Boards, as follows: Forest Products Research—Sir Edward Salisbury, director of the Royal Botanic Gardens, Kew, and secretary of the Royal Society, to succeed V. H. Blackman; Fuel Research—Engineer Vice-Adm. Sir Harold Brown, former senior supply officer, Ministry of Supply, to succeed Sir Harold Hartley; Radio Research—Sir Stanley Angwin, chairman of Cable and Wireless, Ltd., to succeed Lt. Col. Sir George Lee.

The first public atomic power exhibit will highlight the Mid-America Exposition at Cleveland, Ohio, May 22–31. The exhibit is being prepared by a group committee, which includes representatives of the Atomic Energy Commission, the Mid-America Exposition, Inc., and The Kellex Corporation, and a special committee headed by J. R. Dunning, scientific director, Columbia University.

One of the features of this exhibit will be a demonstration of "splitting" the uranium atom. For this demonstration, a special instrument is being built by the Technical Associates, Glendale, California, under the direction of J. R. Dunning. This instrument will permit detection of the energy released through an amplifier. The output from the amplifier will be fed to a 20-inch cathode-ray oscilloscope and a 5-foot fluorescent tube for visual demonstration of the "splitting" process. There will also be an illuminated panel showing the resulting chain reaction following the fission and a sound amplifier for audible demonstration. The fission chamber is being built to simulate an actual pile. Another feature will be a demonstration of atomic energy as a source of power. A special power pilot plant, based on preliminary designs of Farrington Daniels, University of Chicago, is being constructed under the technical supervision of C. R. McCullough, director of atomic power, Clinton Laboratory, Oak Ridge, Tennessee, for this purpose.

The exhibit will also include a display of atomic raw materials, as well as atomic energy research instruments, among which will be the first betatron. Supplementary to exhibits of the American Chemical Society and the American Museum of Natural History, comprising 25 panels, which give the over-all picture of the development of atomic energy from its early discovery through the ore and separation stages to its peacetime applications, there will be displays covering radioactive tracers in medical research, industrial benefits, and other pertinent facets of the subject.

A Committee on Geographical Exploration has been established within the Joint Research and Development Board of the Army and Navy. The Committee is charged with responsibility "for the continuing study of means, programs, and plans for the observation and recording of geographic information in regions not normally accessible, in order to promotive and improve the capabilities of the armed services to exploit and cope with environmental conditions wherever necessary." The field of interest of the Committee includes expeditions and field research stations for geographic studies in polar, tropical, desert, and high-altitude areas.

Members of the Secretariat of the Committee are: Sidney Paige, formerly principal geologist, North Atlantic Division, U. S. Army Engineers, executive director; Wallace W. Atwood, Jr., formerly professor of physiography, Clark University, chief of the Topographic Model Section, U. S. Office of Strategic Services, and chief of the Relief Map Division, Army Map Service, deputy director; Lt. Col. Robert B. Simpson, formerly instructor in geography, University of Rochester, and recently Assistant Military Attaché to Brazil; and Lt. Cdr. L. L. Davis, USN, recently on duty with the Chief of Naval Operations.

Make Plans for—

American Oil Chemists' Society, 38th annual meeting, May 20–22, New Orleans, Louisiana.

American Society of Mechanical Engineers, oil and gas power 19th national conference, May 21–24, Cleveland, Ohio.

New England Section, American Society of Plant Physiologists, May 23–24, University of Vermont, Burlington.

Field Conference of Pennsylvania Geologists, May 30–31 and June 1, Lehigh University, Bethlehem, Pennsylvania.

COMMENTS
by Readers

Beginning in 1926 the Prussian Academy of Sciences, Berlin, began publishing its *Nomenclator Animalium Generum et Subgenerum*, edited during its various stages by F. E. Schulze, W. Kükenthal, K. Heider, and R. Hesse. The work appeared by fascicles and continued well into Volume 5; the last part to come to the Smithsonian Library was dated January 27, 1940, and was received May 12, 1941. This part was labeled "Fünfundzwanzigste Lieferung" and took the catalogue through page 3692, ending with the genus *Zaphleges*. This would indicate that there was one more forthcoming part (Lief. 26), perhaps including addenda, to finish the work through the rest of the letter Z. The war may have prevented the publication of this final Lieferung, but I have been unable to ascertain whether or not it ever appeared. Although the *Nomenclator Zoologicus* of the Zoological Society of London, edited by S. A. Neave, appeared complete in four volumes in 1939–40 and partially supplants the German work, there are certain features of the latter that are very useful to taxonomists and editors of zoological publications in checking the availability of generic names and in running down the literature. Any information which *Science* readers, at home or abroad, can furnish regarding the availability of the final part of this publication will be appreciated. (PAUL H. OEHSER, *editor, U. S. National Museum, Smithsonian Institution, Washington, D. C.*)

Biochemical genetics is fast reaching its place alongside firmly established branches of the biological sciences. Spiegelman and Kamen (*Science*, December 20, 1946) add much in confirming the validity of this opinion. Their attack is not the first on the tradition-bound gene theory. In their article they credit several others with similar views, especially Sewall Wright, of the University of Chicago.

They make no mention, however, of an author whose works I wish to point out, if for no other reason than to create an awareness of their existence. In a book published in 1939 by Blakiston, entitled *The biology of the cell surface*, the late Ernest E. Just, of Howard University, attacked the gene theory on the basis that "... ectoplasmic behavior determines the cytoplasmic reactions that lie at the basis of nuclear activity in both normal and abnormal mitosis." This book contains a large amount of data and much evidence for his theory, and much of what Just says substantiates and supports the Spiegelman-Kamen theory. Many other similarities exist in Dr. Just's complete works. (JAMES H. M. HENDERSON, *The George Washington Carver Foundation, Tuskegee Institute, Alabama.*)

During the course of a routine examination of littoral Octopoda from the western Atlantic in the collections of the British Museum, the undersigned discovered an animal that is apparently hermaphroditic. This specimen was referred to "*Polypus occidentalis* (Steenstrup M. S. Hoyle)" by A. L. Massy (*Zoology*, 1916, **2**, 141–175) and to "*Octopus* (*Octopus*) *rugosus* Bosc" by C. G. Robson (*A monograph of the Recent Cephalopoda*. Pt. I: *Octopodinae*. London: 1929). Both authors regarded it as a female. There can be little doubt that it is a small specimen of *Octopus vulgaris* Lamarck, in accordance with the discovery that neither "*occidentalis*" nor "*rugosus*" from the western Atlantic can be regarded as distinct species (G. E. Pickford. *Trans. Com. Acad. Arts Sci.*, 1945, **36**, 701–777). The specimen, which bears the museum number B.M. 1919. 12.30.40, was taken between tide marks on the shore of the Island of South Trinidad by the "Terra Nova" Expedition. It has a mantle length of 31 mm. A summary of its taxonomic characters is included in a report, now being prepared, on littoral Octopoda from the central and western Atlantic in the collections of the British Museum. Time did not permit as thorough an examination as might be desired, although it is hoped that this may be attempted at some later date. In the meantime the following note is offered in view of the special interest of the specimen. The writer is not aware that hermaphroditism has been observed previously in the Cephalopoda although, of course, it is well known among other groups of mollusks. Moreover, in *Sepia*, according to G. Montalenti and G. Vitagliano (*Publ. Staz. Zool. Napoli*, 1946, **20**, 1–18), the development of the hectocotylus is apparently concomitant with the onset of spermatogenesis, although there is no evidence of hormonal control (H. G. Callan. *Publ. Staz. Zool. Napoli*, 1939, **18**, 15–19).

In the specimen under investigation there is absolutely no evidence of hectocotylization. All arms, with the exception of the second right, which is perfect, have been damaged at their very extreme tips but had already healed before the time of capture, and in two cases, the right first and fourth, minute regenerates are developing. It is hardly likely that damage to the extreme tip of the third left arm could have completely obscured all evidence of hectocotylization; one would suppose that the spermatophoral groove would remain, even if the ligula were lost.

Because of the absence of a hectocotylus, Massy regarded the specimen as a female. However, dissection of the mantle chamber, in an attempt to determine the size of the ovarian eggs, revealed the presence of spermatophore glands. There is no penis, but left and right oviducts are present on either side of the rectum; their connections with the male system were not examined. The male internal genitalia appear to be otherwise quite normal, and the remains of two small spermatophores in Needham's organ prove that the spermatophore glands are functional. The gonad was not examined histologically to determine whether it contained ovarian as well as testicular tissue.

The observations recorded above appear to indicate that the secondary sexual characters of Cephalopoda are not subject to hormonal control.

The writer would appreciate receiving information regarding the possible occurrence of other hermaphroditic specimens. (GRACE E. PICKFORD, *Osborn Zoological Laboratory* and *Bingham Oceanographic Laboratory, Yale University.*)

TECHNICAL PAPERS

Properties of Adsorbed Chlorophyll

H. C. EYSTER

Charles F. Kettering Foundation, Antioch College, Yellow Springs, Ohio

Most of the investigations on chlorophyll have been done in solution in such fat solvents as ether, ethanol, methanol, acetone, etc. As such, the chlorophyll is deep green in color, shows much red fluorescence, and is rapidly decomposed by light.

In the experiment described in this preliminary report, chlorophyll in solutions of acetone and ethanol was adsorbed on charcoal (norit A), talc, fuller's earth, infusorial earth, casein, agar, gelatin, Ottawa sand, absorbent cotton, filter paper, calcium carbonate, egg albumin, cornstarch, and supercel. No attempt was made to purify the chlorophyll solution, to separate the extraction mixture into *a* and *b* components, or to remove the carotenoids.

The best method of adsorbing chlorophyll from a solution was that used by Willstätter and Stoll (*2*), who adsorbed chlorophyll onto the surface of talc from an acetone solution. The chlorophyll in dry, powdered nettle leaves was extracted in 80 per cent acetone. Talc (about 1 gram to each 50 ml. of acetone solution) and then distilled water were added to dilute the acetone to 55 per cent. Upon standing (2–15 hours) and filtering, the talc residue on the filter paper was thoroughly washed with distilled water and was observed to have a deep green color, comparable to the color of many leaves. As the talc dried, the color became much lighter, as it does in leaves as they are dried. The dried talc with a green coating of chlorophyll is quite comparable in physical appearance to the powder of dried nettle leaves.

Charcoal is very effective in adsorbing chlorophyll from a diluted solution. Although it was the most effective adsorbent of those tried, it has the disadvantage of remaining black in color. Also, chlorophyll cannot be eluted from charcoal surfaces with the ordinary solvents, such as acetone, ethanol, methanol, ether, etc. According to the author's present knowledge, pyridine is the only substance which will do so.

Talc, fuller's earth, infusorial earth, cotton, supercel, and egg albumin have proved to be quite effective adsorbents of chlorophyll in 55 per cent acetone. The egg albumin was dissolved in water and then added to acetone to make a 55 per cent aqueous solution of acetone, from which the egg albumin precipitated. Sand may be just as effective if the amount of chlorophyll is correlated with surface. Casein and gelatin are somewhat less effective and have the disadvantage of becoming hardened into a tough, brittle, plastic-like material from which there can be no easy extraction of the chlorophyll. Agar, which is about the poorest adsorbent, loses what little chlorophyll it adsorbs when the agar residue is washed to remove the acetone. Calcium carbonate, cornstarch, and filter paper are also rather poor. The frayed edges of the filter paper are much more effective.

The best adsorbents are talc, fuller's earth, infusorial earth, and adsorbent cotton. These substances, when moist with water, take on the green leaf-like color and, when dry, resemble the light green color of dried leaf powder. Furthermore, except for cotton, which was used in its usual fibrous form, they retain their powdered form. The chlorophyll in all four cases can be re-extracted as easily as it is extracted from whole leaves or from such material as finely powdered, dry nettle leaves. Of these four, talc seems to be the best.

The properties of chlorophyll adsorbed on these adsorbents are very much like those of chlorophyll in the leaf, as found by Fishman and Moyer (*1*). The adsorbed chlorophyll has a natural green color, a reddish fluorescence, an electronegative charge, and great photostability. The reddish fluorescence was observed in the dark by irradiating a suspension of chlorophyll-coated talc in distilled water with ultraviolet light from a Cenco ultraviolet light source. The fact that chlorophyll adsorbed on talc, as well as chlorophyll in living cells, displays a red fluorescence is a crucial indication that chlorophyll in its natural state is adsorbed on the surface of chloroplast material, most likely the grana.

TABLE 1

ABSORPTION SPECTRA OF CHLOROPHYLL IN VARIOUS AQUEOUS DILUTIONS OF ACETONE

Acetone (%)	Absorption bands			
	First*	Second*	Third*	Fourth*
80, 75, 70	6825–6360 (6593)	6230–6030 (6130)	5875–5675 (5775)	5435–5295 (5365)
65	6895–6365 (6630)	6260–6050 (6155)	5895–5680 (5788)	5460–5310 (5385)
60	6915–6400 (6658)	6270–6070 (6170)	5915–5705 (5810)	5480–5350 (5415)
55	6950–6425 (6688)	6290–6070 (6180)	5900–5705 (5803)	5485–5340 (5413)
50	6940–6440 (6690)	6285–6070 (6178)	5895–5690 (5793)	5500–5350 (5425)
40	6870–6445 (6658)	6280–6090 (6185)	5900–5675 (5788)	5485–5360 (5423)
20	6845–6480 (6663)	Shadow		5485–5370 (5428)
10	6810–6490 (6650)			Shadow

* Averages are in parentheses.

Another important property of adsorbed chlorophyll is the similarity of its absorption spectrum with that of chlorophyll in living leaves. A study of the absorption spectra of chlorophyll in 80, 75, 70, 65, 60, 55, 50, 40, 20, and 10 per cent acetone shows that there is a shift in the position of the absorption bands between approximately 70 and 55 per cent. The shift begins slightly above 70 per cent acetone, and continues gradually and in direct proportion to any dilution between 70 and 55 per cent, becoming complete at 55 per cent (Table 1). This characteristic seems to indicate why 55 per

cent acetone is the most effective dilution from which to adsorb chlorophyll on talc or any other adsorbent.

The total shifts in the bands are: 95 A. for the first, 50 A. for the second, 27 A. for the third, and 47 A. for the fourth.

Upon successive dilutions, ethyl alcohol (95 per cent) extract of chlorophyll from fresh green corn leaves shows the same shift of the absorption bands toward the red end of the spectrum: 98 A. for the first, 52 A. for the second, 27 A. for the third, and 57 A. for the fourth. A 95 per cent ethanol extract of chlorophyll from dry nettle leaves does not show a shift in the spectrum upon dilution with water, probably because of allerimization.

The reason for the shift in the spectrum as a result of dilution with water is not known definitely, but it appears that it may be due to the adsorption of (or the chemical union with) water on the surface of the chlorophyll molecule.

The absorption spectrum of chlorophyll adsorbed on the different adsorbents moistened in water is quite similar to that of chlorophyll in 55 per cent acetone or in solutions with less percentage of acetone. There is a shift toward the red end of the spectrum, quite similar to that in living leaves. The absorption spectra of chlorophyll on dry talc and on dry cotton show no change in position of the bands as compared with that of adsorbed chlorophyll on water-moistened talc and cotton. Thus, the water which possibly originally caused the shift may be retained and may be the principal factor causing the chlorophyll to adhere to talc, cotton, or any adsorbent.

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Daily Nitrogen Urinary Excretion in People of the Working Class of Caracas

FRANCISCO DE VENANZI

Departamento de Patología General y Fisiopatología, Instituto de Medicina Experimental, Universidad Central de Venezuela

Studies on the elimination of nitrogen and on nitrogen balances are as old as the science of nutrition. The first investigators who involved themselves in these problems had the opportunity of working with very exact methods, and many of their results fit perfectly into the science of today. The work of Boussingault (*3*), Liebig (*10*), Bidder and Schmidt (*1*), and especially Voit and his collaborators (*11*) showed the relationship between nitrogen ingestion and eliminated nitrogen. The notion of nitrogen ingestion equilibrium was established.

It is well known not only that the diet of the Venezuelan people is poor in high-protein-content foods and especially low in proteins of rich biological value (*5*), but also that total serum proteins in the popular class are low, resulting in a high incidence of hypoproteinemia (*7*), especially during pregnancy (*4*) and lactation (*6*). For this reason it seemed interesting to establish the daily urinary excretion of nitrogen, this being the most exact procedure available for determining the amount of metabolized proteins in the body. These determinations were recommended by the International Conference of Berlin in 1932 (*12*) as a very accurate measure of protein intake, although, as Bigwood (*2*) stated, it is sometimes difficult to obtain a complete sample.

For the whole group it was found that 53 per cent of the determinations were under the average value, and 85 per

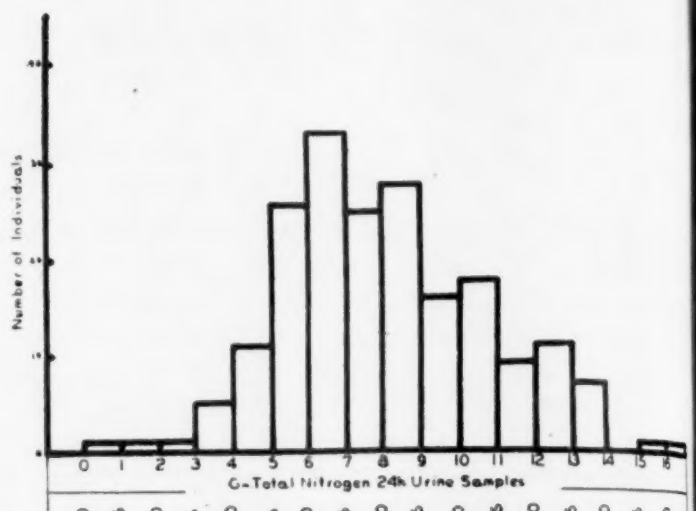

FIG. 1

cent eliminated less than 11 grams of nitrogen in the urine over a period of 24 hours.

METHODS

Determinations were made of total nitrogen in urine eliminated over a period of 24 hours by 194 apparently healthy people attending the Health Certificate Service. Of these, 118 were females and 76 were males. The ages ranged from 11 to 57 years, but the majority were young adults. Special care was taken in order to obtain complete

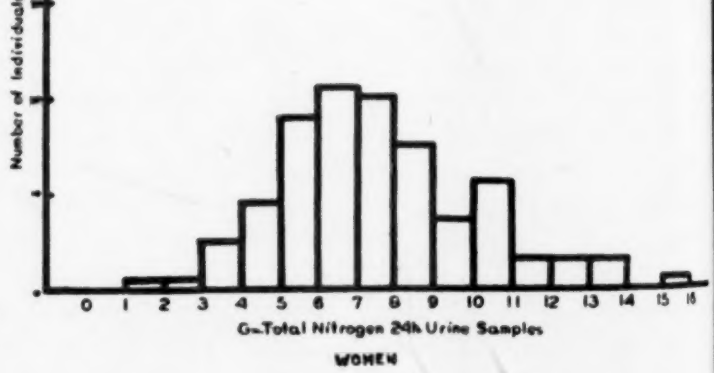

FIG. 2

24-hour samples. The subjects were notified that daily elimination is greater than one liter, and bottles for the purpose were provided. Samples suspected of being incomplete were rejected. Determinations of creatinine were made in all the samples. In a group of 37 women eliminating less than one liter of urine the average creatinine value was the same as that in a group of 92 women eliminating more than one liter. The variation coefficient was smaller in the first group. Almost all the men eliminated more than 1,000 cc. of urine,

The amount of urine in the samples was carefully measured. The found average for the whole group was 1.066 cc. with a S.D. 1.42. The determinations of total nitrogen were

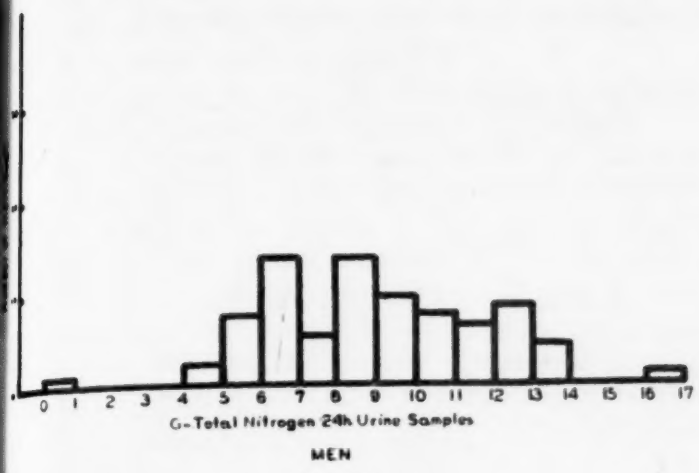

FIG. 3

made with the macro-Kjeldahl technique (*9*), using Gunning's modification (*8*). The determinations, carried out in duplicate in 80 per cent of the cases, checked well.

RESULTS

The histograms for the whole group, the female group, and the male group are shown in Figs. 1, 2, and 3, respectively. In Fig. 1 the values are expressed in grams of nitrogen and in calculated metabolized proteins (N × 6.25). Table 1

TABLE 1

	No. Individuals	Averages (grams N/day)	S.D.	N × 6.25	Modes (grams N/day)
Whole group.....	194	8.03	2.80	50.2	6–7
Female	118	7.46	2.56	46.6	6–7
Male.....	76	8.89	2.74	55.6	6–9

shows the averages, standard deviations, calculated metabolized protein corresponding to the averages, and the modes of the distributions of the found values.

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Heterologous Transplantation of Human Tumors

MACHTELD E. SANO

Agnes Barr Chase Surgical Research Foundation, Temple University School of Medicine and Hospital, Philadelphia

Two human tumors of the same type, both questionable lymphosarcomata or leukemias, were transplanted into mice after passage through tissue culture. One animal developed a tumor which metastasized to the liver and was identical to the human tumor. Another developed a similar tumor at the site of inoculation, but the cells infiltrated the adjacent breast tissue, initiating in it an adenocarcinoma which metastasized rapidly. Another mouse presents a leukemic picture with an absolute white count of 37,000. The suspected lability of these difficult-to-diagnose lymph-node tumors is thus experimentally demonstrated. Preliminary passage through tissue culture permitted transplantation of the human tumor to the animal without previous passage through the anterior chamber of the eye.

Inhibition of Heating and Lipolysis in Seeds

MARJORIE Z. CONDON, F. R. ANDREWS
MADELINE G. LAMBOU, and A. M. ALTSCHUL[1]

Southern Regional Research Laboratory,[2] New Orleans, Louisiana

Heating and deterioration of moist seeds has constituted a problem in those processing industries where seeds must be stored in bulk for extended periods of time. Damage resulting from heating is manifested not only by visible discoloration of the seeds but also by reduction of the quantity and quality of the processed products. For example, cottonseed which has been damaged by heating during storage will yield less oil than prime cottonseed, and the oil which is obtained will contain an increased percentage of free fatty acids.

Heating in seeds during commercial storage is minimized by one of the following procedures: (1) predrying prior to storage, (2) forced aeration during storage, or (3) stacking bagged seeds in a manner that provides natural circulation of air in the interspaces. Reduction or prevention of deterioration may also be effected by treating the seeds with chemicals to inhibit the biological processes which are responsible for heating and deterioration (*1*, *3*, *4*, *5*). An investigation has been made to determine the effectiveness of a wide variety of chemicals as such inhibitors. Preliminary results of this survey are presented here, and detailed reports on the calorimetric method used and its application to problems of seed storage will appear elsewhere.

[1] The authors wish to acknowledge the invaluable aid given them by the many chemical manufacturers who suggested and furnished many of the compounds tested to date. The free fatty acid determinations were made by Miss Claire Lesslie.

[2] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

The test is performed by placing seeds, which have been artificially moistened and treated with the chemical whose inhibitory power it is desired to test, into calibrated Dewar flasks and drawing air through them at a rate which will support maximum heating. The temperature within the seeds is determined periodically by means of a thermocouple and manually-operated or recording potentiometer. After one week of storage under these conditions, the seeds are removed from the flasks and examined for other evidence of deterioration, e.g. content of free fatty acids in the case of oil seeds.

To compensate for differences in biological activity resulting from variations in age, history, variety, and type of sample, the response of the seeds treated with any chemical or group of chemicals is compared simultaneously with an untreated sample of the same seed having the same moisture content, and with a sample of the same seed having the same moisture content but which had been treated with a standard quantity of ethylene chlorhydrin.

Response curves obtained in a typical experiment are shown in Fig. 1. In this graph the effect of treating flaxseed conditioned to 22 per cent of moisture (wet basis) with different concentrations of diethyl oxalate is compared with the standard ethylene chlorhydrin treatment. A concentration

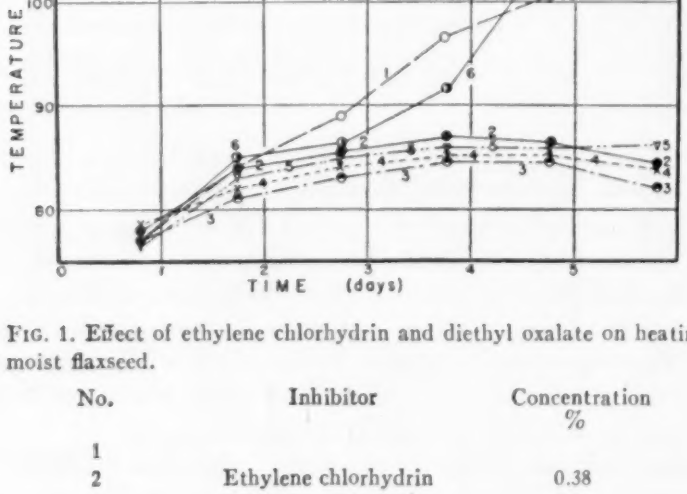

FIG. 1. Effect of ethylene chlorhydrin and diethyl oxalate on heating of moist flaxseed.

No.	Inhibitor	Concentration %
1		
2	Ethylene chlorhydrin	0.38
3	Diethyl oxalate	0.35
4	" "	0.28
5	" "	0.24
6	" "	0.16

of 0.24 per cent[3] diethyl oxalate was found to inhibit heating as effectively as 0.38 per cent ethylene chlorhydrin. It should be noted that treatment of the seed with 0.16 per cent diethyl oxalate stimulated the evolution of heat so that temperatures above that of the untreated control were observed. As will be shown (Table 1), the latter concentration of diethyl oxalate also stimulated lipolysis. The phenomenon of stimulation or inhibition as a function of concentration has been repeatedly observed in seed storage investigations (*2–4*) and appears to be an inherent property of many substances normally considered as inhibitors (*7*). After the seeds have been in the Dewar flasks for 6 days, they are removed and analyzed for free fatty acids content. The results of determination of free fatty acids corresponding to the calorimeter data in Fig. 1 are recorded in Table 1, from which it is apparent that diethyl oxalate is more effective as an inhibitor of heating than of lipolysis.

TABLE 1

EFFECT OF TREATMENT OF MOIST FLAXSEED WITH DIETHYL OXALATE AND ETHYLENE CHLORHYDRIN ON DEVELOPMENT OF FREE FATTY ACIDS IN THE SEED OIL

Inhibitor	Concentration* (%)	Free fatty acid content† (%)
None		3.65
Ethylene chlorhydrin	0.38	0.79
Diethyl oxalate	0.35	1.05
" "	0.28	1.63
" "	0.24	2.20
" "	0.16	4.88

* Weight of inhibitor per weight of dry seed.

† Free fatty acids content of original seeds, 0.78 per cent; free fatty acids determined after storages for 6 days.

By the use of the above-illustrated method it has been possible to determine the concentration of inhibitor which will give approximately the same degree of inhibition as the standard concentration of ethylene chlorhydrin. All of the chemicals have, therefore, been tested in concentrations of approximately 0.38 per cent. Those which had less activity than ethylene chlorhydrin when applied in this concentration were rejected, while those exhibiting activity equal to or better than the

TABLE 2

RELATIVE EFFECTIVENESS OF VARIOUS CHEMICALS AS INHIBITORS OF HEATING AND LIPOLYSIS IN FLAXSEED

Chemical	Effect on lipolysis		Effect on heating	
	Concentration equivalent to 0.38% ethylene chlorhydrin (%)*	Relative effectiveness†	Concentration equivalent to 0.38% ethylene chlorhydrin (%)*	Relative effectiveness†
1-Chloro-1-nitroethane	0.42	0.9	0.42	0.9
8-Quinolinol	0.42	0.9	0.42	0.9
Orthovanillin	0.42	0.9	0.42	0.9
Phenol	0.32	1.2	0.32	1.2
Benzotrichloride	0.45	0.85	0.45	0.85
p-tert-Amyl phenol	0.42	0.9	0.42	0.9
Salicylaldehyde	0.26	1.5	0.38	1.0
1,3-Dimethyl-4,6-bis(chloromethyl)benzene	0.032	12.0	‡	‡
Ethylene bromhydrin	0.18	2.1	0.18	2.1
Sodium cyanide	0.042	9.0	0.017	23.0
Propylene glycol dipropionate	0.26	1.5	0.26	1.5
Diethyl oxalate	>0.38	<1.0	0.24	1.4
Chloramine-T	<0.11	>3.5	‡	‡

* Weight of inhibitor per weight of dry seed.

† Compared to 0.38 per cent ethylene chlorhydrin as 100.

‡ These compounds did not affect the heating of the seeds in the same manner as did ethylene chlorhydrin and were, therefore, not given a relative rating.

[3] Concentration is expressed in terms of weight of inhibitor per dry weight of treated seeds.

standard inhibitor were tested further at several other concentrations. Since there was no a priori reason to expect that the inhibitors would be equally effective on heating and lipolysis, the relative efficiency of each inhibitor was determined with respect to both effects. The comparative effectiveness of a series of chemicals is shown in Table 2.

The data reveal the fact that a wide variety of chemicals in fairly low concentrations are capable of inhibiting heating and lipolysis in moist flaxseed.[4] Although flaxseed was used in all of the experiments, a number of the inhibitors listed in Table 2 have also been used in treating moist cottonseed, rice, and grain sorghum and have been found to be equally effective. The low concentrations at which many of these compounds were effective as inhibitors of heating and lipolysis suggest their use in treating seeds on an industrial scale to improve their storage properties. Mill-scale experiments to determine the effectiveness of a number of these inhibitors are in progress.

No attempt is made here to interpret the results presented above in terms of the relation between chemical structure and biological activity of the compounds examined to date. It is probable that although their net effect, namely, inhibition of heating and lipolysis, is the same, the mechanism whereby this inhibition is achieved in the seed may differ for each inhibitor. It is necessary, therefore, to investigate their effect on the components of the enzyme systems involved in heating and lipolysis before any conclusions can be drawn regarding the relationship between chemical structure and biological activity.

Other investigators (e.g. *6*) have attributed the heating and deterioration of grain to the action of microorganisms associated with the grain. As has been pointed out in a previous publication (*4*), heating and deterioration can be equally well ascribed to the enzyme activity within the seeds themselves. It is also possible that the enzymes both in the seeds and in the microorganisms are responsible, perhaps in different degrees, for the observed biological activity of the seeds. It has not been possible to conclude definitely what relative role is played by the enzymes from the two sources.

The objective of this research has been to develop improved methods of storage of seeds intended for industrial or food utilization in which preservation of viability is not important. It is recognized that the development of improved conditions for the storage of planting stock constitutes an equally important problem, and it is hoped that some of the results of these investigations may eventually be applied in storing seeds without loss of viability.

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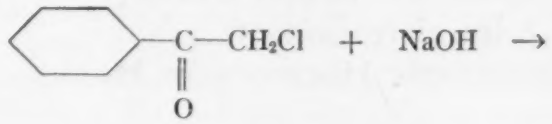
[4] In addition to the chemicals listed in Table 2, calcium propionate, glycol diacetate, diethyl malonate, and vinyl propionate have recently been found to act as inhibitors when used in concentrations equivalent to that of the ethylene chlorhydrin standard.

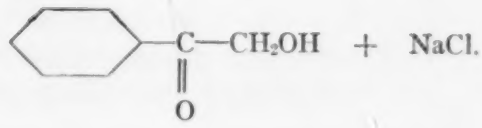
Hydrolysis by Carbitolic Caustic

R. Macy

Chemical Corps Technical Command, Edgewood Arsenal, Maryland

Chloracetophenone (CN) has long been a popular lacrimator both for military and civilian uses. For example, it is a standard component of grenades employed by civilian police as well as by military forces. CN is characterized by rather high chemical stability, so that decontamination of an area covered by it can be accomplished by relatively few chemical treatments. One of the favorite points of attack on the molecule is the chlorine atom through hydrolysis by alkali:





Since CN is practically insoluble in water, the hydrolysis must be accomplished by employing the caustic in a solvent which will also dissolve the CN. Such a solvent is ethanol. A solution consisting of 5 per cent of sodium hydroxide and 95 per cent of ethanol will destroy a thin film of CN on a contaminated surface in a few minutes.

Because of the fire hazard introduced by ethanol in this decontaminating agent in certain military operations, a search was made for other mutual solvents for CN and sodium hydroxide. An added requirement for the solvent was that it should have good stability toward the alkali when the solution was stored. A large number of solvents were tested, and the search finally led to the following series of compounds:

(I)	$HOCH_2CH_2OH$	Ethylene glycol
(II)	$HOCH_2CH_2OCH_2CH_3$	Cellosolve
(III)	$HOCH_2CH_2OCH_2CH_2OH$	Diethylene glycol
(IV)	$HOCH_2CH_2OCH_2CH_2OCH_2CH_3$	Carbitol
(V)	$HOCH_2CH_2OCH_2CH_2OCH_2CH_2OH$	Triethylene glycol

As a result of these tests it was found that compound IV stood out quite sharply, not only for its solvent capacity for organic compounds but also for its stability toward alkali. The solubility of CN in dry carbitol at 22° C. was found to be 28.3 grams in 100 grams of solution, and in a mixture of 21 per cent of water and 79 per cent of carbitol (by weight) it was 9.3 grams in 100 grams of solution.

A solution containing, by weight, 5 per cent sodium hydroxide, 20 per cent water, and 75 per cent carbitol hydrolyzes CN quite rapidly when in thin film on an area. (In granular form CN dissolves rather slowly in carbitol, although it dissolves to a large extent, as already stated.) Higher concentrations of caustic can be used to give more rapid hydrolysis, but concentrations over 5 per cent may cause skin injuries unless personnel are well protected. The 5 per cent caustic solution in aqueous carbitol was found to be stable for at least two years in a sealed steel drum stored in the open without

cover. It turns red on standing and absorbs the oxygen from the air in the container.

The principal object of this report is to bring carbitolic caustic to the attention of laboratory workers as a possible replacement for the well-known alcoholic caustic. There are probably many circumstances under which it should be a more desirable reagent. It is relatively nonflammable and can be used at temperatures considerably higher than the boiling point of ethanol if required to decompose a compound under reflux conditions.

Changes in Urinary Steroid Excretion and Correlated Metabolic Effects During Prolonged Administration of Adrenocorticotropic Hormone in Man[1]

GEORGE W. THORN, F. T. GARNET PRUNTY,[2] and PETER H. FORSHAM

Department of Medicine, Harvard Medical School, and *Medical Clinic, Peter Bent Brigham Hospital, Boston*

Adrenocorticotropic hormone was administered to a 46-year-old male, known to have an expanding lesion involving the sella turcica which had been arrested by roentgen therapy. This subject was chosen because of the presence of signs and symptoms of moderate secondary adrenal-cortical insufficiency, which could be expected to accentuate any adrenotropic response to the pituitary hormone.

The adrenocorticotropic hormone was prepared from hog pituitary glands.[3] Two gamma of this preparation was found to give an adrenotropic response in the assay method of Sayers and Sayers (*1*). Electrophoretic analysis revealed the presence of more than one component. The material contains the equivalent of 0.12 unit of oxytocic activity/mg.; growth-promoting, gonadotropic, and thyrotropic factors are not present in significant amounts.

The patient was maintained on a constant diet and, after reaching a steady state, was given intramuscular injections of 10 mg. of A.C.T.H. every 6 hours for 6 days (40 mg. daily).

Some of the metabolic effects observed are shown in Fig. 1, in which the following changes should be noted: A 7-fold increase in the daily excretion of "11-oxysteroids," as estimated by a modification of the method of Talbot, *et al.* (*2*); an accompanying 5-fold increase in the 17-ketosteroid excretion; an increase of 58 per cent in the daily urinary output of total nitrogen, with a concurrent rise in the excretion of uric acid. Urinary creatinine remained constant from day to day. The excretion of sodium was markedly decreased throughout the period of administration.

The marked increase in the excretion of "11-oxysteroids" may be taken as definite evidence of increased adrenal-cortical activity under the action of the A.C.T.H. used. The rise in 17-ketosteroid output to as high a figure as 12.2 mg./day would indicate that the major part of this material was, in fact, derived from the adrenal cortex, since the maximum output by

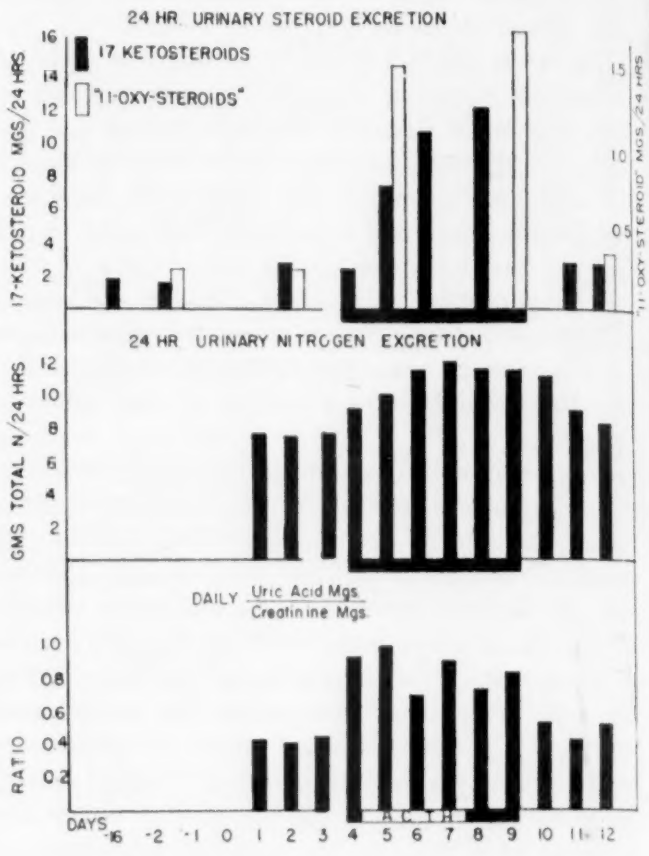

24 HR. URINARY STEROID EXCRETION
17 KETOSTEROIDS
"11-OXY-STEROIDS"
17-KETOSTEROID MGS./24 HRS.
"11-OXY STEROID" MGS./24 HRS.
24 HR. URINARY NITROGEN EXCRETION
GMS. TOTAL N/24 HRS.
DAILY Uric Acid Mgs. / Creatinine Mgs.
RATIO
DAYS
-3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12
A.C.T.H.

FIG. 1

even normal testes is only of the order of 5 mg./day. The simultaneous changes observed in the excretion of both types of urinary steroid may be taken in support of either of two hypotheses: (1) that 17-ketosteroids derived from the adrenal cortex are formed to a considerable extent by the oxidative removal of the side chains of C_{21} steroids, the production of the latter being controlled by A.C.T.H.; or (2) that the anterior pituitary gland, through its A.C.T.H., stimulates the independent production of both C_{21} steroids and 17-ketosteroids, or related androgens, by the adrenal cortex.

The increased nitrogen excretion parallels that of the "11-oxysteroids," which are known to promote the catabolism of body protein, whereas the sodium retention suggests the elaboration of a desoxycorticosterone-like substance. From the close correlation between the observed changes in the urinary excretion of steroids, nitrogen, and uric acid, it appears useful to regard the ratio of uric acid to creatinine as a measure of increased activity of the adrenal cortex during a period of stimulation. This has been confirmed by experiments, being reported elsewhere, which include the demonstration that patients with primary adrenal-cortical insufficiency fail to show this response.

[1] This study was aided in part by a grant from the Committee on Research in Endocrinology, National Research Council.

[2] Rockefeller Traveling Fellow.

[3] We are indebted to J. R. Mote, of the Armour Company, for a supply of the adrenocorticotropic hormone prepared in the Armour Laboratories.

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Method for Measuring the Speed of Centrifuges

F. R. HUNTER and J. F. HOFFMAN[1]

Department of Zoology, University of Oklahoma, Norman

The method to be described has been used to measure the speed of rotation of an air turbine.[2] It can be modified, however, to measure the speed of most rotating objects and so may be used in many instances where a tachometer or stroboscope is not readily available.

The principle is very simple and direct: A soot-covered surface is moved parallel to the axis of rotation so that each revolution is recorded; simultaneously, a record of the rate of rotation of a tuning fork is obtained on the same surface. Fig. 1 illustrates the metal frame (in this instance, brass) used

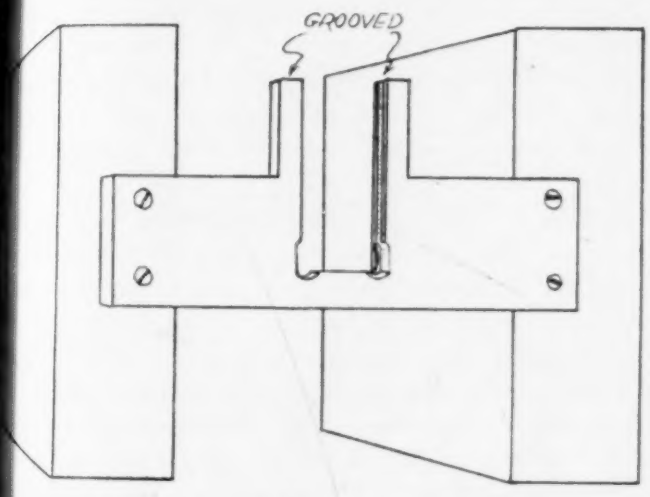

FIG. 1. Frame for holding microscope slide.

to guide the movement of the sooted surface. The two vertical supports are grooved to hold a microscope slide. The horizontal support is fastened to a wooden block on each end so that the upper surface of the rotor is a short distance below the upper end of the microscope slide when it is in place in the brass frame. For recording, a fiber is glued (using speaker-cone cement) in a horizontal position on the upper surface of the rotor so that it extends ¼ inch beyond the periphery. A similar fiber is glued to the tuning fork. The choice of fibers may be varied, but a portion of a bristle from an eraser brush was found to be satisfactory for several tracings. A small length of phosphor bronze wire would be more durable. In order to reduce the deformation of the fiber, since at very high speeds there might be insufficient time for a markedly bent fiber to return to its initial position, a glass rod is sealed lengthwise to the microscope slide with De Khotinsky cement.

The tuning fork need not be mounted to make the measurements, although a simple support could easily be made if desired. Both surfaces of the microscope slide (including the rod) are blackened, and it is placed in the metal frame with the rod side toward the turbine. The rotor is started, and the frame is moved close enough so that the fiber just marks on the rod. The tuning fork is started and touched to the plain surface of the slide, which is pulled up out of the frame. Measurements are then made on the two sides of the slide. If one makes both measurements, starting from the marks made before the slide is moved, the tuning fork does not have to be lined up with the fiber on the rotor. No error is introduced by acceleration of the slide. If a more rapid rate of slide movement is required, the frame could easily be modified to incorporate a rubber band or spring to be substituted for hand pulling. Velocities of 300 r.p.s., using a tuning fork of 512 c.p.s., were measured easily without any conscious effort to pull the slide rapidly.

[1] Acknowledgment is due Dr. Hans Weltin, Department of Physics, University of Oklahoma, who suggested the method and constructed the apparatus.

[2] One of the authors (F. R. H.) is indebted to the Faculty Research Fund of the University of Oklahoma for this piece of apparatus.

A Biologically Absorbable Surgical Glove Powder

JOHN T. CORRELL and E. C. WISE

Research Laboratories, The Upjohn Company, Kalamazoo, Michigan

These investigations were initiated by increasing emphasis in the medical literature (*2*) that talc as a glove powder has serious limitations and that a nonirritating, biologically absorbable substitute might be indicated.

Our experience with the controlled heat denaturation of gelatin (*1*) led us to investigate the possibility of rendering gelatin flour relatively water insoluble yet amenable to ***in vitro*** proteolytic digestion. Such alteration of the protein molecule might yet leave it susceptible to phagocytosis and hence biologically absorbable by the tissues.

Finely ground gelatin was subjected to electric oven heating at 145° C. for the periods of time indicated in Table 1. The protein became progressively less soluble in water at room temperature. In addition to nitrogen analysis of the supernatants, a practical test of the relative tackiness of each fraction on the damp hands indicated that solubility approached a minimum after about 25 hours of heating.

TABLE 1

PROTEOLYTIC DIGESTION OF PROGRESSIVELY DENATURED GELATIN

Heating time (hrs.)	0	4	20	25	29	45	93
Pepsin digestion time (min.)	10	5	15	25	55	90	135

The ***in vitro*** proteolytic digestion of these heat-denatured protein fractions was ascertained as follows: A solution was prepared by dissolving 2 grams of U.S.P. pepsin in 100 cc. of 0.37 per cent HCl. To 100 mg. of the protein was added 100 ml.

of this pepsin solution, and the flask suspended with agitation in a constant temperature bath at 37° C. When by visual examination with transmitted light no solids could be seen in suspension upon vigorous agitation, the protein was considered digested. The data in Table 1 show that with prolonged dry heating (dehydration ?) of the protein powder it becomes less readily lysed by enzymatic action—a property which paralleled the physical phenomenon of decreasing water insolubility.

Gelatin powders such as those which were heated 25 hours or longer have been injected into the peritoneal cavities of rats for preliminary investigations. Animals sacrificed after 4–5 weeks showed no granulomata or adhesions; no trace of the injected gelatin powder was in evidence.

Since several of these denatured protein fractions appeared to serve satisfactorily as a rubber glove powder for lubrication, the physiological aspect of this problem is being investigated further and will be reported later in greater detail.

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A Method of Drying Partial Protein Hydrolysates and Other Hygroscopic Materials for Nutritional Studies

R. J. Westfall, O. Miller, and I. S. Westfall

Department of Biochemistry, Medical Research Division, Sharp & Dohme, Inc., Glenolden, Pennsylvania

Drying a protein hydrolysate by lyophilization is a procedure that often is desirable as a means of preparing diets for studies of the nutritive value of the hydrolysate. Unfortunately, the tendency to fuse during lyophilization and the hygroscopic nature of the dry material detract from the usefulness of the lyophile technique for this purpose. It has been found in this laboratory that these difficulties are overcome largely by concentrating the solution *in vacuo* and adding dextrin to the concentrated solution. Of the common dietary carbohydrates, only dextrin or starch is suitable; sucrose or cerelose does not aid in subsequent lyophilization.

The vacuum concentration of protein hydrolysates is difficult with ordinary types of distillation apparatus because of the severe foaming usually experienced. With an apparatus of the type described by Mitchell, Shildneck, and Dustin (*1*), distillation rates up to 5 l./hour may be attained at temperatures below 50°C., without any antifoaming agent. An efficient condenser is necessary. A copper water-heater coil, surrounded by a water jacket, was found to be convenient and adequate for this purpose. With this apparatus typical hydrolysates were concentrated to at least 50 per cent solids.

The concentrated hydrolysate is placed in bottles, and dextrin is added and mixed by shaking, after which shelling and lyophilizing are carried out in the usual way. The volume of hydrolysate in each bottle should not be over 10 per cent of the total volume of the bottle. In this laboratory, sufficient dextrin is added to give 30–50 per cent protein in the dry product. The lyophilized material is easily powdered for incorporation in diets.

The same procedure is useful in drying hygroscopic materials, such as liver extract, for use in experimental diets.

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Synergistic Insecticides

Herman W.

Research Department, Dodge & Olcott, I. Bayonne, New Je

During the recent war an added war had to be fought against an army of insects in order to keep our fighting men from falling prey to disease. In this connection the well-known freon-propelled "aerosol" bomb (*3*) made its appearance. Since the end of the war the ease of handling and effectiveness of this bomb have caught the public's fancy, and it may be expected that it will be used as an additional weapon in the expanding war on insects on the home front.

Contrary to some popular misconceptions, the rapidity of knockdown action of the "aerosol" bomb on insects has been due solely to the presence of pyrethrins, which have the unique property of quickly paralyzing insects and other cold-blooded animals while being innocuous to warm-blooded animals.

Because of the high cost of the pyrethrins, many attempts have been made to replace them, and the patent literature of the last few years describes a host of synthetic organic compounds which are highly toxic to insects. None of these, however, possesses the outstanding property of the pyrethrins.

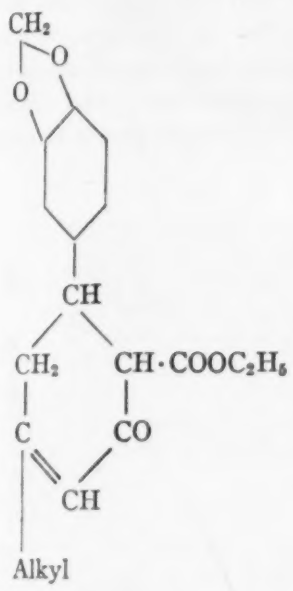
A more promising approach was initiated through the interpretation by Haller and his co-workers of the discovery by Eagleson (*1*) that the addition of sesame oil to pyrethrum extracts increased their effectiveness (*4*). These investigators linked the increased effectiveness with the synergistic effect of the sesamin present in the oil and later with the presence of a methylene-dioxy-phenyl group in the sesamin. They subsequently synthetized the amides of 3,4-methylene-dioxy cinnamic acid and found them active as synergists with pyrethrins (*2*).

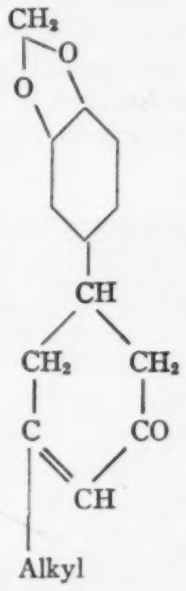
These products, however, did not find practical application because of the difficulty of preparing them in quantity and because of their limited solubility in freon and in petroleum hydrocarbons, which are used as vehicles for insecticidal sprays.

O. F. Hedenburg, of the Mellon Institute, Pittsburgh, has been independently investigating compounds containing the methylene-dioxy-phenyl group as insecticides. The results with the chemicals alone did not appear too promising because of the poor knockdown property of the compounds, but when they were tested in combination with pyrethrins, a different result was obtained. While the majority of the compounds tested, including safrole and isosafrole, esters, etc., displayed little or no activity, a new product with outstanding activity was discovered. This was obtained by the condensation of the alkyl-3,4-methylene-dioxy-styryl ketones with ethyl acetoacetate (*5*). The insecticidal effect of this product is appar-

from the fact that a solution of 300 mg. of this substance in combination with 30 mg. of pyrethrins in 100 cc. of odorless base oil gave 99 per cent knockdown and 90 per cent kill of houseflies when tested according to the Peet-Grady method (*8*); 30 mg. of pyrethrins dissolved in 100 cc. of odorless base oil will give a knockdown of a little better than 80 per cent and a kill of about 15 per cent; 300 mg. of the condensation product dissolved in 100 cc. of odorless base oil will, under the test conditions, give a knockdown of less than 10 per cent and therefore practically no kill.

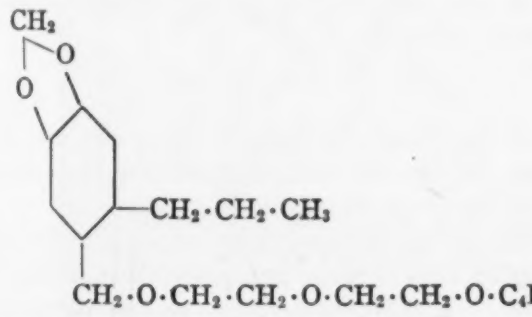
The technical reaction product found prompt commercial acceptance under the name "piperonyl cyclohexenone." It was subsequently found (*6*) to contain 80 per cent of a mixture of





in addition to higher molecular condensation products.

Although the physical characteristics of "piperonyl cyclohexenone" made it satisfactory enough to be useful in insecticidal sprays in conjunction with secondary solvents, the search was intensified for a product of increased activity and of complete miscibility with freon and with petroleum hydrocarbons. (3,4-Methylene-dioxy-6-propyl benzyl) (butyl) diethylene-glycol ether



was synthetized in this laboratory (*7*) and found to possess the desired properties. This also shared with the pyrethrins the property of being practically nontoxic to warm-blooded animals (M.L.D.: 7.5 grams/kg.). The product boils at 180° at 1 mm. It is a colorless liquid, soluble in all the common organic solvents.

The activity of piperonyl butoxide (the name given the technical product containing 80 per cent of pure compound) is indicated in Table 1. The tests were run according to the established Peet-Grady procedure (*8*) by dissolving the indicated quantities of piperonyl butoxide and pyrethrins in 100 cc. of odorless base oil.

While it is apparent that we still have no substitute available for pyrethrins, it is now possible to employ the latter in a very much lower concentration and to obtain effectiveness which would be uneconomical, if at all feasible, if pure pyrethrins were used. It is gratifying that the addition of the synergist does not introduce toxicological hazards.

TABLE 1

Pyrethrins (mg.)	Piperonyl butoxide (mg.)	Knockdown	Kill
20	100	93	62
20	200	96	77
20	400	97	84
30	100	95	59
30	200	97	77
30	400	99	92
40	100	97	74
40	200	98	82
40	400	97	90
40	0	84	34
100	0	95	46
0	300	8	—

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Specific Surfaces of Bone, Apatite, Enamel, and Dentine

Noel V. Wood, Jr.[1]

Department of Radiology, School of Medicine and Dentistry, University of Rochester

Recently a few preliminary measurements were made of the specific surfaces of some tooth and bone samples and of a synthetic hydroxylapatite.[2] In making the determination, small samples of the four powders were weighed in sample bulbs and the bulbs sealed into the vacuum system. The whole teeth were washed with distilled water and acetone and sealed in bulbs on the apparatus. The system was evacuated to approximately zero pressure and the samples heated for about two hours at 200° C. to drive off any condensed moisture or gases. After this initial operation, the adsorption determination was carried out to obtain several points on the iso-

[1] Present address: Hydrocarbon Research, Inc., Trenton, New Jersey.

[2] The apatite was prepared in this laboratory (*3*). The bone was glycol-ashed rabbit bone (*2*). The dentine and enamel were samples from human teeth prepared in the powdered form by the Manly-Hodge method (*4*).

The author acknowledges the kindness of Robert C. Likins and Miss Marlene Falkenheim, of the University of Rochester School of Medicine and Dentistry, who furnished the tissue samples.

therm curve. Exact details of the procedure cannot be enumerated, but many detailed procedures of gas adsorption methods are described in the literature (*1*).

The results of the tests are given in Table 1. It was impossible to obtain exact values for the whole teeth because not a single

TABLE 1

Sample	Approximate particle size	Wt. of sample (grams)	Total surface (sq. cm.)	Specific surface (sq. m./gram)
Apatite		0.0098	5,002	51.1
Dentine	60 mesh	0.0192	461.7	2.4
Enamel	60 "	0.0196	352.8	1.8
Bone ash	60 "	0.0089	8,835	99.3
Tooth #2		1.2845	22,000*	1.77*
Tooth #3		1.0528	16,700*	1.59*

* Estimation.

equilibrium pressure-volume point necessary for the isotherm could be obtained during a continuous 8-hour determination. The most probable reason for the failure to obtain equilibrium points was the unusually large size of the samples.

The surface area results on the powders are amazing. For example, bone ash has about 100 sq. m. of surface/gram. The variation of specific surface between bone, apatite, dentine, and enamel is of special interest because these were of the same particle size (*i.e.* 60 mesh). Presumably these variations revealed differences in the sizes of the submicroscopic crystals of hydroxylapatite.

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Increasing the Spreading Coefficient of Mustard Gas[1]

Walter H. C. Rueggeberg

Chemical Corps Technical Command, Edgewood Arsenal, Maryland

It is a well-known fact that small amounts of so-called "capillary active agents," when added to water, greatly reduce the surface tension of that liquid. As a result of this phenomenon, it was assumed that the addition of a low percentage of an appropriate soluble wetting agent to mustard gas (hereafter referred to as H) would reduce its surface tension to such an extent that the interfacial tension between it and water would be reduced sufficiently to increase the spreading coefficient beyond its normal value of 1 to 4.[2] To this end, several of the commercially available wetting agents were tried. Unfortunately, however, most of these, due to their high polarity, were insoluble in H and consequently, in this investigation, Alkaterge-O[3] was used throughout in order to establish the validity of the initial premise. The mustard gas was prepared from thiodiglycol and hydrochloric acid (m.p., 14.25°; purity, 99.5%). Distilled water having a surface tension of 72.0 dynes at 26° was used.

The mathematical reasoning involved in the theory of the spreading of liquids is adequately covered in textbooks on physical chemistry (*1*).

Procedure

All measurements were made by means of the Du Nuoy interfacial tensiometer. All equipment, including the ring, was carefully cleaned in chromic acid. The ring was heated in a Bunsen flame before insertion into its seat in the apparatus. No attempt was made to control the temperature to an accuracy greater than ±1°, since the aim was to find tension differences far greater than those encountered over a 1° range in temperature. Readings were taken at room temperature of about 24°–26°. The results, averaging from about 6 to 8 separate readings, are compiled in Table 1.

TABLE 1

Surface and Interfacial Tensions of H, the System H-H_2O With and Without Alkaterge-O, and the Spreading Coefficient of H Calculated From These Values*

System	Alkaterge-O (%)	Surface tension in air, γ (dynes/cm.)	Interfacial tension (γ AB, dynes/cm.)†	Calculated spreading coefficient of H on water (γB-γA-γAB)
H_2O	0	72.0	—	—
H	0	40.6	23.0‡	+8.4§
H	½	33.2	about 6.0	+32.9
H	1	31.7	" 1.0	+39.3
H	2	31.6	" 1.0 max.	+39.4
H	5	31.4	" 1.0 max.	+39.6

* All values are corrected by means of calibration curve.

† A = surface tension of H; B = surface tension of H_2O; AB = interfacial tension of the system H-H_2O.

‡ A value of 28.4 dynes/cm. at a lower temperature is on record in an Edgewood Arsenal report.

§ A value of +1.6 has been previously recorded for a lower temperature in an Edgewood Arsenal report.

It is apparent from the data presented that the surface and interfacial tensions of H can be lowered through the addition of 1 per cent of a surface active agent such as Alkaterge-O. The lowering of the tensions is sufficient to increase the spreading coefficient considerably above the value obtained with untreated H.

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[1] Published with the permission of the Chief, Chemical Corps.

[2] Taken from reports on file at Edgewood Arsenal.

[3] An amine of high molecular weight, obtainable from the Commercial Solvents Corporation, New York City. According to the analysis performed in the Edgewood Laboratories, the empirical formula is $C_{22}H_{18}O_2NH_4$.